

9-1215

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Scientific and Technical Information Center

SEARCH REQUEST FORM

Requester's Full Name: SABINA GAZD Examiner #: 74141 Date: 9/22/06
 Art Unit: 1616 Phone Number: 2-0622 Serial Number: 101821,479
 Location (Bldg/Room#): 4A45 (Mailbox #): 4C70 Results Format Preferred (circle): PAPER DISK

Raw

To ensure an efficient and quality search, please attach a copy of the cover sheet, claims, and abstract or fill out the following: ME

Title of Invention: 2-Propylidene-19-nor-Vitamin D compounds
 Inventors (please provide full names): DeLuca et al

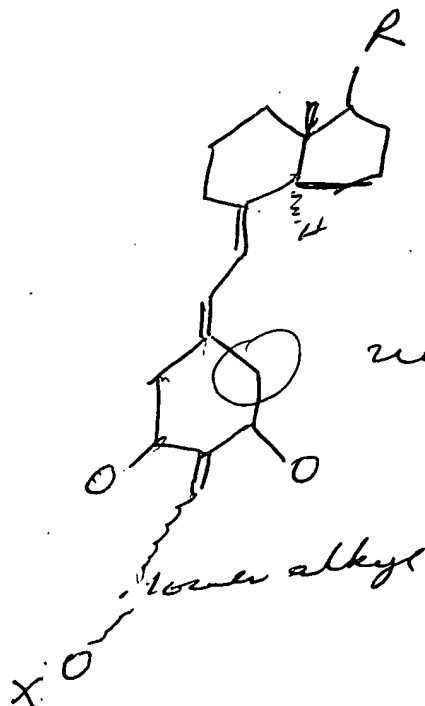
Earliest Priority Date: 4/10/2003

Search Topic:

Please provide a detailed statement of the search topic, and describe as specifically as possible the subject matter to be searched. Include the elected species or structures, keywords, synonyms, acronyms, and registry numbers, and combine with the concept or utility of the invention. Define any terms that may have a special meaning. Give examples or relevant citations, authors, etc., if known.

For Sequence Searches Only Please include all pertinent information (parent, child, divisional, or issued patent numbers) along with the appropriate serial number.

Please search for ^{19-nor} Vit D compounds of Cl 1
 and their method of use



Broad Search

no 19 CH₂ gp (called 19-nor)
Vit D

For Specific Compds
 See Compds of Cl 12-16.

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E VITAMIN D/CN

E VITAMIN D 19-NOR/CN

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L8 6 S L7

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L16 8 S L15 AND L2

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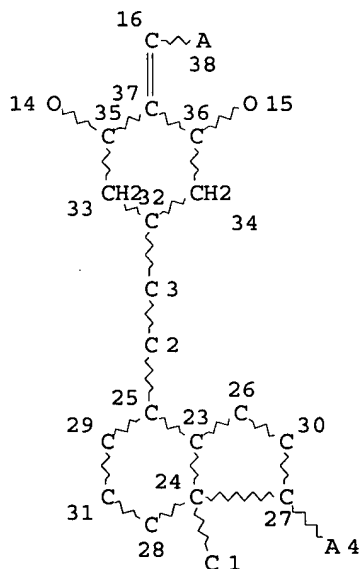
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DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS 23

STEREO ATTRIBUTES: NONE

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L17 4 SEA FILE=HCAPLUS ABB=ON PLU=ON L16

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L17 ANSWER 1 OF 4 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2006:376695 HCAPLUS
DOCUMENT NUMBER: 145:83577

TITLE: New 2-Alkylidene 1 α ,25-Dihydroxy-19-norvitamin D3 Analogues of High Intestinal Activity: Synthesis and Biological Evaluation of 2-(3'-Alkoxypropylidene) and 2-(3'-Hydroxypropylidene) Derivatives

AUTHOR(S): Glebocka, Agnieszka; Sicinski, Rafal R.; Plum, Lori A.; Clagett-Dame, Margaret; DeLuca, Hector F.

CORPORATE SOURCE: Department of Biochemistry, University of Wisconsin-Madison, Madison, WI, 53706, USA

SOURCE: Journal of Medicinal Chemistry (2006), 49(10), 2909-2920
CODEN: JMCMAR; ISSN: 0022-2623

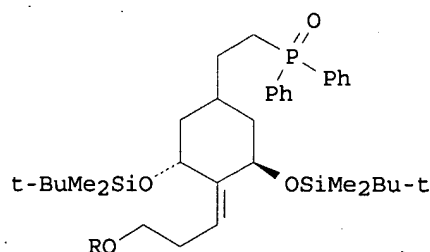
PUBLISHER: American Chemical Society

DOCUMENT TYPE: Journal

LANGUAGE: English

OTHER SOURCE(S): CASREACT 145:83577

GI



AB In a search for novel vitamin D compds. of potential therapeutic value, E- and Z-isomers of 1 α ,25-dihydroxy-2-(3'-hydroxypropylidene)-19-norvitaminD3, as well as a derivative of the former compound possessing a 3'-(methoxymethoxy)propylidene substituent at C-2, were efficiently prepared. All vitamins were obtained in convergent syntheses, starting with (-)-quinic acid and the protected 25-hydroxy Grundmann ketones. Phosphine oxides I were prepared and subjected to Lythgoe type Wittig-Horner coupling with CD-ring fragments. An alternative route was also elaborated that comprised Julia coupling of sulfones with a cyclohexanone derivative. The binding of all synthesized vitamins to the full-length rat recombinant vitamin D receptor (VDR) is either similar to or within one log of 1 α ,25(OH)2D3. The in vivo tests have revealed that the calcemic activity of all analogs in the E-series is considerably higher than that of the native hormone.

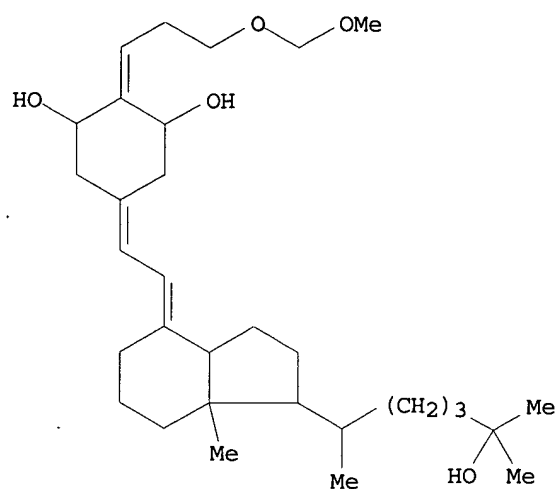
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781664-71-9P 781664-72-0P

RL: PAC (Pharmacological activity); PRP (Properties); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)

(preparation and biol. evaluation of 2-alkoxypropylidene and 2-hydroxypropylidene 1 α ,25-dihydroxy-19-norvitamin D3 analogs)

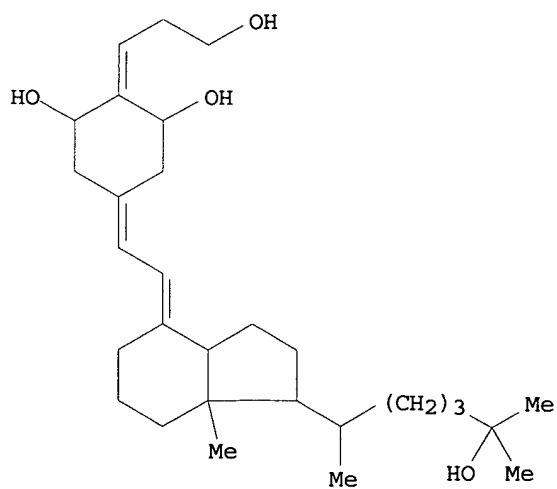
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(9CI) (CA INDEX NAME)



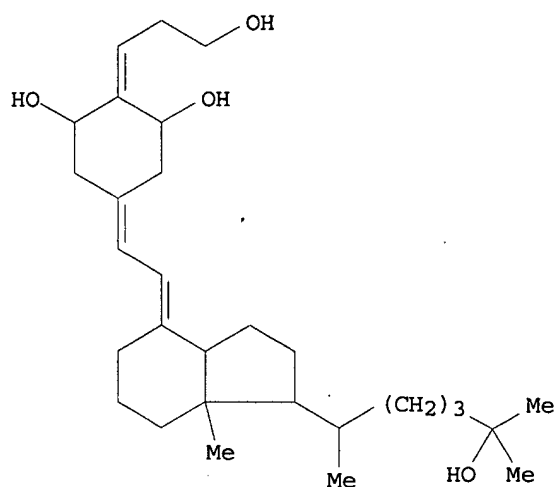
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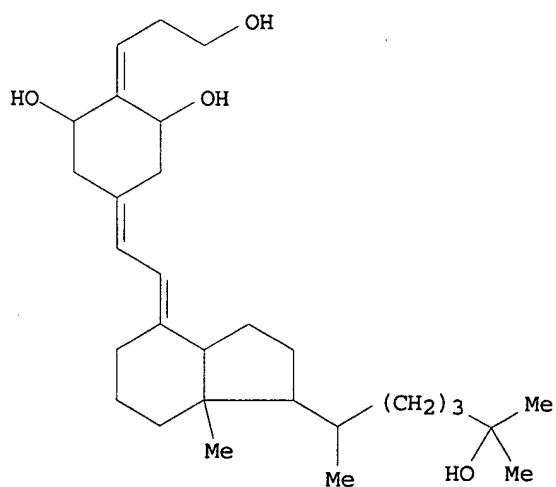


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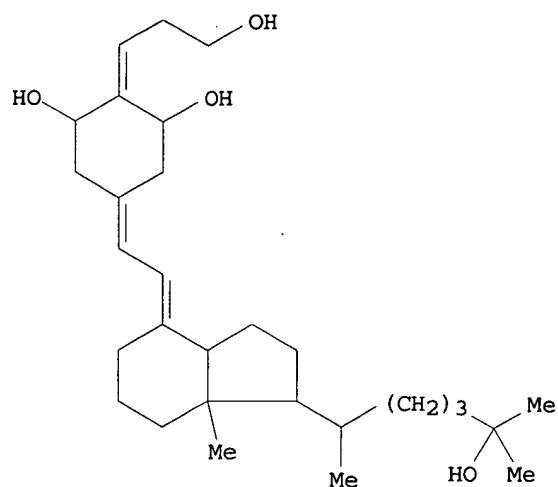
CN 19-Nor-9,10-secocholesta-5,7-diene-1,3,25-triol,
2-(3-hydroxypropylidene)-, (1 α ,2Z,3 β ,7E)-(9CI) (CA
INDEX NAME)



RN 781664-71-9 HCAPLUS
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 2-(3-hydroxypropylidene)-, (1 α ,2E,3 β ,7E,20S)- (9CI)
 (CA INDEX NAME)



RN 781664-72-0 HCAPLUS
 CN 19-Nor-9,10-secocholesta-5,7-diene-1,3,25-triol,
 2-(3-hydroxypropylidene)-, (1 α ,2Z,3 β ,7E,20S)- (9CI)
 (CA INDEX NAME)

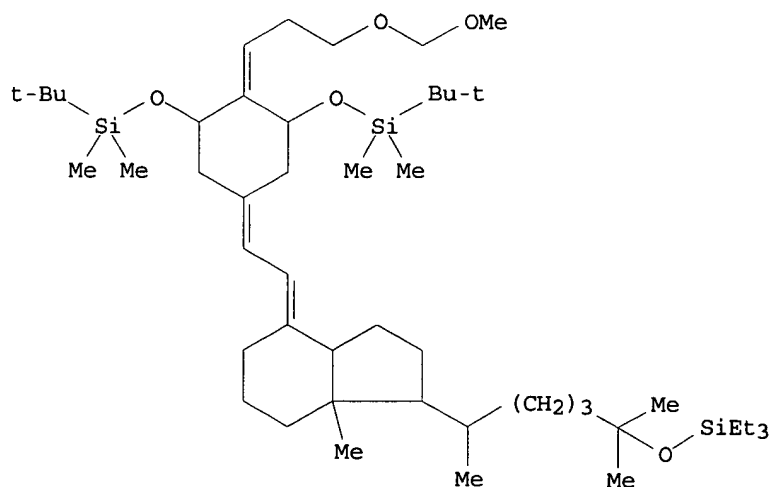


IT 766529-93-5P 781664-39-9P 781664-70-8P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and biol. evaluation of 2-alkoxypropylidene and 2-hydroxypropylidene 1 α ,25-dihydroxy-19-norvitamin D3 analogs)

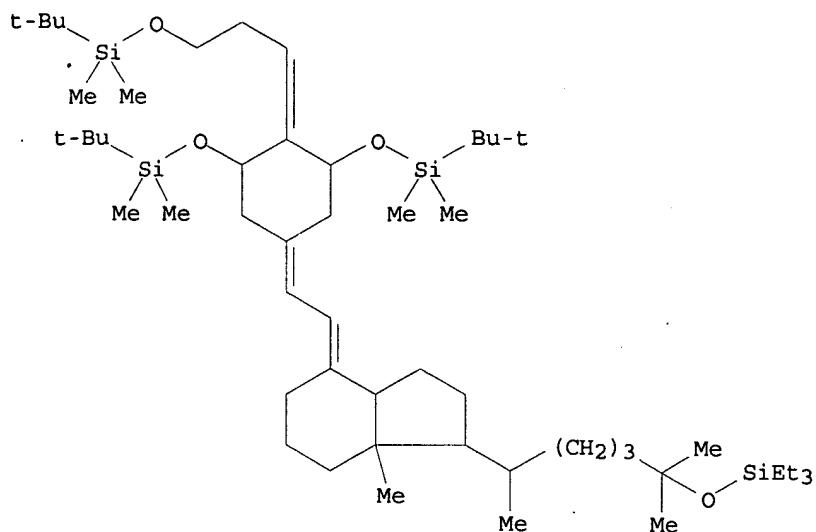
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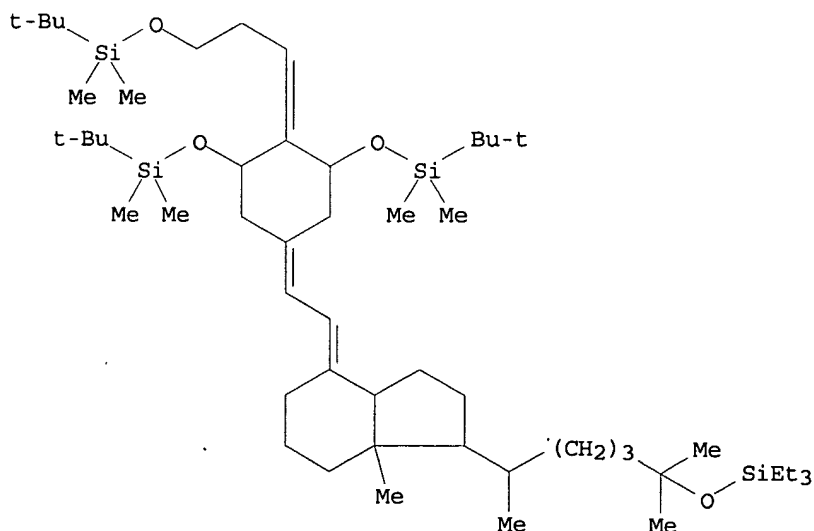
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RN 781664-70-8 HCAPLUS

CN Silane, [[(1 α ,2E,3 β ,7E,20S)-2-[3-[[[(1,1-dimethylethyl)dimethylsilyl]oxy]propylidene]-25-[(triethylsilyl)oxy]-19-nor-9,10-secocholesta-5,7-diene-1,3-diyl]bis(oxy)]bis[(1,1-dimethylethyl)dimethyl-(9CI) (CA INDEX NAME)



CC 32-7 (Steroids)

Section cross-reference(s): 2

IT 766529-87-7P 781664-40-2P 781664-41-3P
781664-71-9P 781664-72-0P

RL: PAC (Pharmacological activity); PRP (Properties); SPN
(Synthetic preparation); BIOL (Biological study); PREP
(Preparation)

(preparation and biol. evaluation of 2-alkoxypropylidene and
2-hydroxypropylidene 1 α ,25-dihydroxy-19-norvitamin D3
analogs)

IT 78365-43-2P 120379-76-2P 163217-18-3P 194227-13-9P

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RL: RCT (Reactant); SPN (Synthetic preparation); PREP
 (Preparation); RACT (Reactant or reagent)
 (preparation and biol. evaluation of 2-alkoxypropylidene and
 2-hydroxypropylidene 1 α ,25-dihydroxy-19-norvitamin D3
 analogs)

REFERENCE COUNT: 36 THERE ARE 36 CITED REFERENCES AVAILABLE
 FOR THIS RECORD. ALL CITATIONS AVAILABLE
 IN THE RE FORMAT

L17 ANSWER 2 OF 4 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2005:474934 HCAPLUS

DOCUMENT NUMBER: 143:20385

TITLE: Vitamin d analogs for obesity prevention and
 treatment

INVENTOR(S): Deluca, Hector F.; Clagett-Dame, Margaret;
 Ahrens, Jamie M.; Ntambi, James M.; Thomson,
 Brian

PATENT ASSIGNEE(S): Wisconsin Alumni Research Foundation, USA

SOURCE: U.S. Pat. Appl. Publ., 102 pp.

CODEN: USXXCO

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

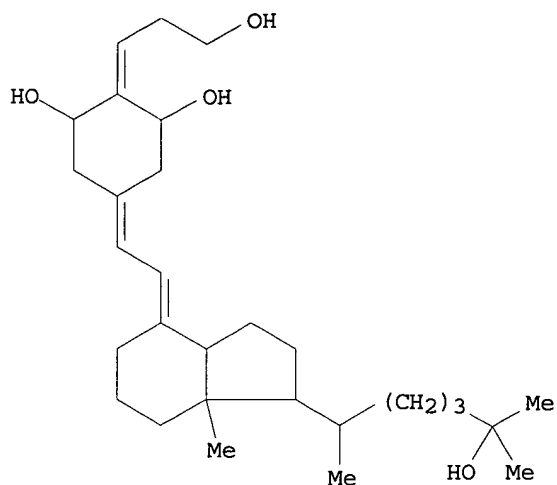
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AU 2004293092	A1	20050609	AU 2004-293092	2004 1124
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WO 2005051396	A2	20050609	WO 2004-US39524	2004 1124
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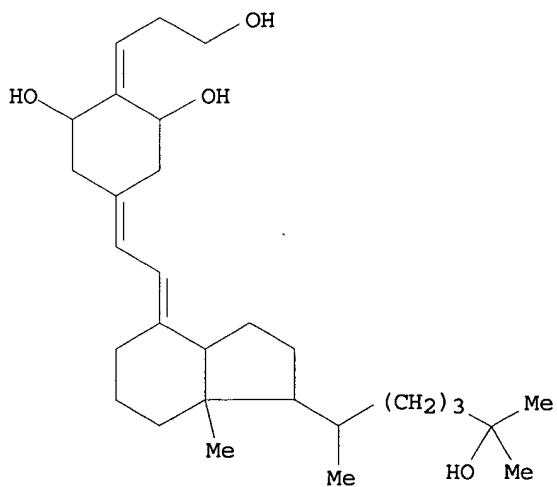
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OTHER SOURCE(S): MARPAT 143:20385

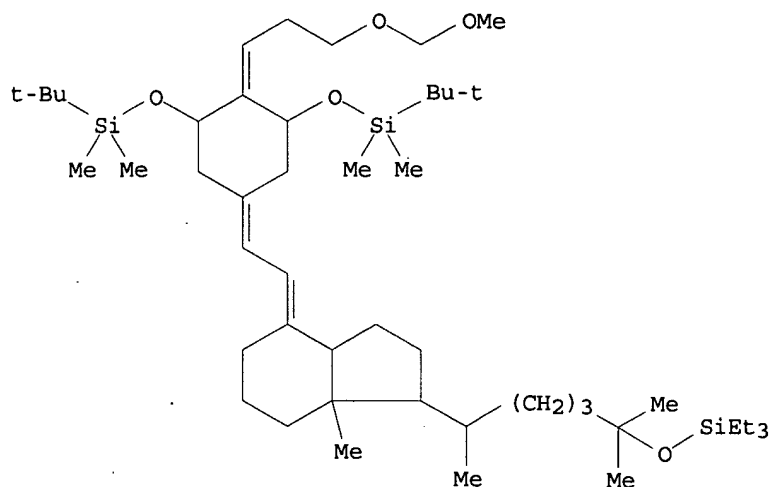
AB Methods for treating and preventing obesity, inhibiting adipocyte
 differentiation, inhibiting increased SCD-1 gene transcription,
 and/or reducing body fat in a subject include administering at
 least one analog of 1 α ,25-dihydroxyvitamin D₃,
 1 α ,25-dihydroxyvitamin D₂, or 19-nor vitamin D or a
 pharmaceutical composition that includes such an analog to a subject in
 need thereof are disclosed.
 IT 781664-41-3P 781664-72-0P
 RL: PAC (Pharmacological activity); SPN (Synthetic preparation);
 THU (Therapeutic use); BIOL (Biological study); PREP
 (Preparation); USES (Uses)
 (vitamin D analogs for obesity prevention and treatment)
 RN 781664-41-3 HCAPLUS
 CN 19-Nor-9,10-secocholesta-5,7-diene-1,3,25-triol,
 2-(3-hydroxypropylidene)-, (1 α ,2Z,3 β ,7E)- (9CI) (CA
 INDEX NAME)



RN 781664-72-0 HCAPLUS
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 (CA INDEX NAME)

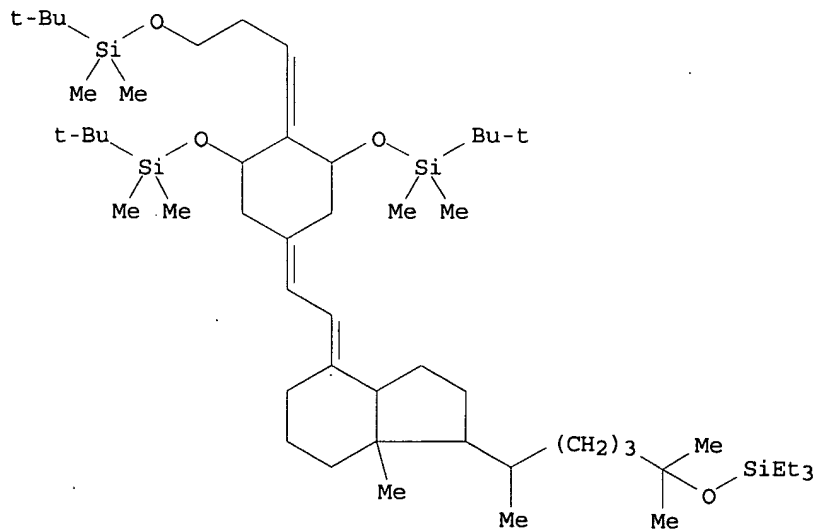


IT 766529-93-5P 781664-39-9P 781664-70-8P
 RL: RCT (Reactant); SPN (Synthetic preparation); PREP
 (Preparation); RACT (Reactant or reagent)
 (vitamin D analogs for obesity prevention and treatment)
 RN 766529-93-5 HCAPLUS
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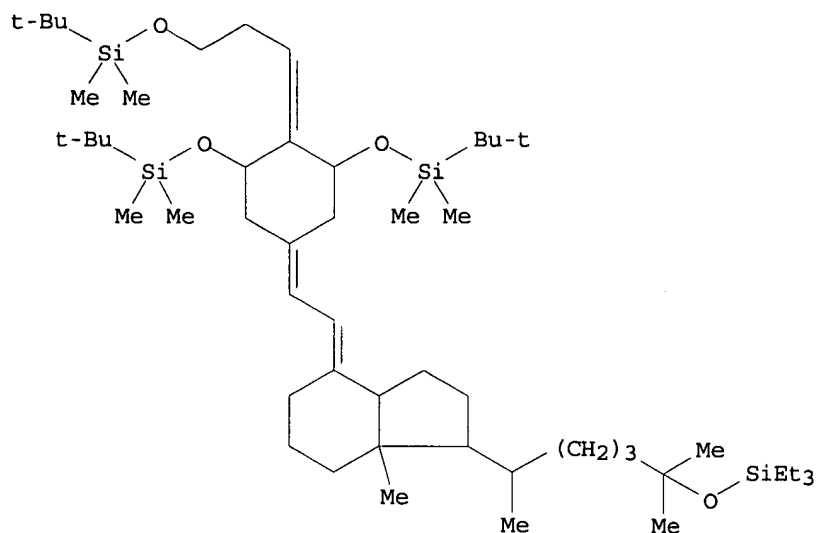
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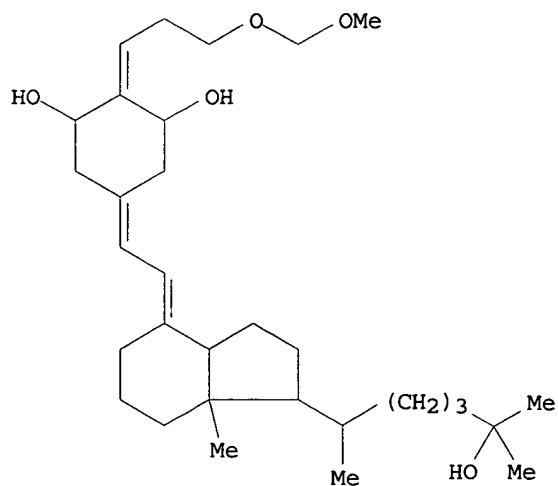


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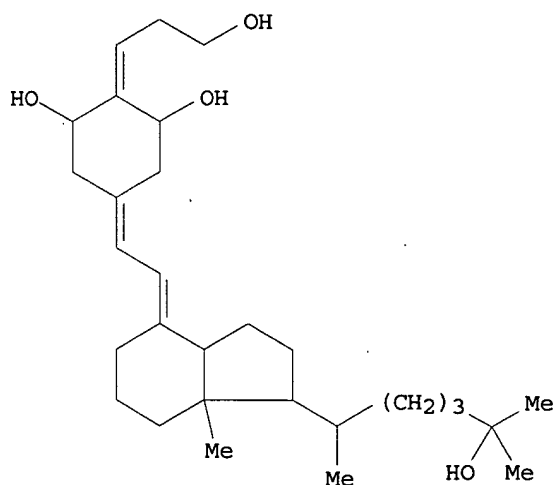
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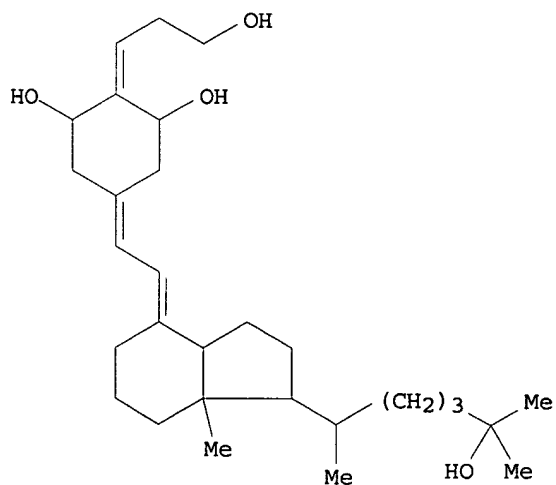
IT 766529-87-7 781664-40-2 781664-71-9
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 (vitamin D analogs for obesity prevention and treatment)
 RN 766529-87-7 HCAPLUS
 CN 19-Nor-9,10-secocholesta-5,7-diene-1,3,25-triol,
 2-[3-(methoxymethoxy)propylidene]-, (1 α ,3 β ,6E,7E)-
 (9CI) (CA INDEX NAME)



RN 781664-40-2 HCAPLUS
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 2-(3-hydroxypropylidene)-, (1 α ,2E,3 β ,7E)- (9CI) (CA
 INDEX NAME)



RN 781664-71-9 HCAPLUS
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 2-(3-hydroxypropylidene)-, (1 α ,2E,3 β ,7E,20S)- (9CI)
 (CA INDEX NAME)



IC ICM A61K031-59
 INCL 514167000
 CC 2-10 (Mammalian Hormones)
 Section cross-reference(s): 1, 63
 IT 213250-70-5P 524067-20-7P 524067-21-8P 524067-22-9P
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 RL: PAC (Pharmacological activity); SPN (Synthetic preparation);
 THU (Therapeutic use); BIOL (Biological study); PREP
 (Preparation); USES (Uses)
 (vitamin D analogs for obesity prevention and treatment)
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RL: RCT (Reactant); SPN (Synthetic preparation); PREP

(Preparation); RACT (Reactant or reagent)

(vitamin D analogs for obesity prevention and treatment)

IT 60133-18-8D, 1 α -25-Dihydroxyvitamin D₂, analog 131918-61-1

766529-87-7 781664-40-2 781664-71-9

845815-92-1 852932-01-5 852932-02-6 852932-03-7

RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(vitamin D analogs for obesity prevention and treatment)

L17 ANSWER 3 OF 4 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2004:902336 HCAPLUS

DOCUMENT NUMBER: 141:380071

TITLE: Preparation of 2-propylidene-19-norvitamin D compounds for pharmaceutical use

INVENTOR(S): Deluca, Hector F.; Sicinski, Rafal R.; Glebocka, Agnieszka; Plum, Lori A.

PATENT ASSIGNEE(S): Wisconsin Alumni Research Foundation, USA

SOURCE: PCT Int. Appl., 91 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

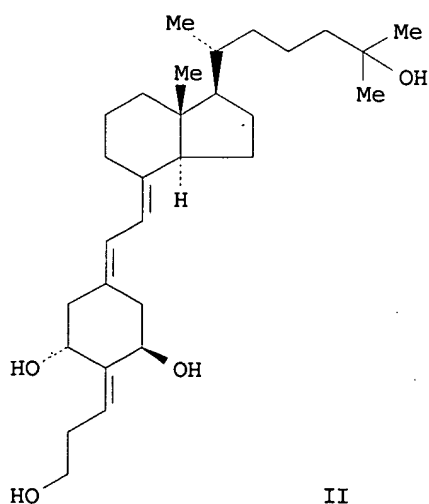
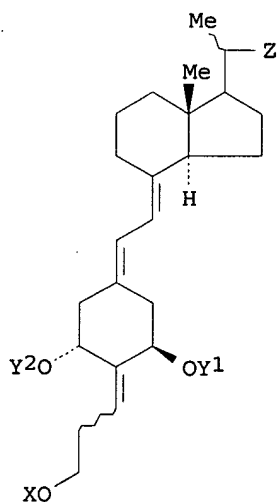
FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004092118	A2	20041028	WO 2004-US11059	2004 0409
WO 2004092118	A3	20050127		
W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW			
RW:	BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG			
AU 2004230948	A1	20041028	AU 2004-230948	2004 0409

CA 2516233	AA	20041028	CA 2004-2516233	2004 0409
US 2004229851	A1	20041118	US 2004-821479	2004 0409
EP 1613588	A2	20060111	EP 2004-749961	2004 0409
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BR 2004009194	A	20060411	BR 2004-9194	2004 0409
CN 1771226	A	20060510	CN 2004-80009620	2004 0409
PRIORITY APPLN. INFO.:				
			US 2003-461958P	P 2003 0410
			US 2004-821479	A 2004 0409
			WO 2004-US11059	A 2004 0409

OTHER SOURCE(S): MARPAT 141:380071
GI



AB 2-Propylidene-19-norvitaminD compds. of formula I [Y1, Y2 = H, protecting group; X = H, alkyl, protecting group, hydroxyalkyl, alkoxyalkyl, aryloxyalkyl; Z = H, Me, acyl, (substituted) OH, CH2OH, etc.] are prepared for pharmaceutical use. These compds. are characterized by high bone calcium mobilization activity and high intestinal calcium transport activity. This results in novel therapeutic agents for the treatment and prophylaxis of diseases

where bone formation is desired, particularly osteoporosis, as well as autoimmune diseases such as multiple sclerosis, diabetes mellitus and lupus. These compds. also exhibit pronounced activity in arresting the proliferation of undifferentiated cells and inducing their differentiation to the monocyte thus evidencing use as an anti-cancer agent and for the treatment of skin diseases such as psoriasis. These compds. also increase both breaking strength and crushing strength of bones evidencing use in conjunction with bone replacement surgery such as hip and knee replacements. Thus, II was prepared and showed significant activity in promoting the differentiation of leukemia cells.

IT 766529-87-7P 781664-40-2P 781664-41-3P

781664-71-9P 781664-72-0P

RL: PAC (Pharmacological activity); SPN (Synthetic preparation);

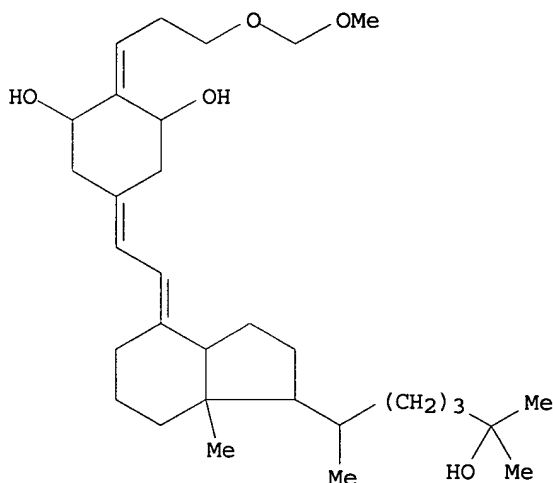
THU (Therapeutic use); BIOL (Biological study); PREP

(Preparation); USES (Uses)

(preparation of 2-propylidene-19-norvitaminD compds. as antiosteoporotics and antitumor agents)

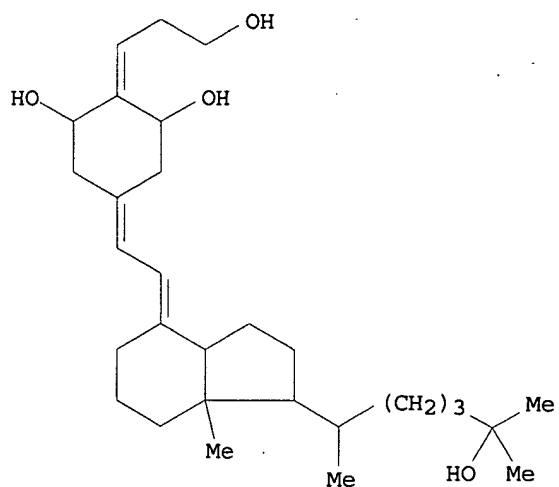
RN 766529-87-7 HCAPLUS

CN 19-Nor-9,10-secocholesta-5,7-diene-1,3,25-triol,
2-[3-(methoxymethoxy)propylidene]-, (1 α ,3 β ,6E,7E)-
(9CI) (CA INDEX NAME)

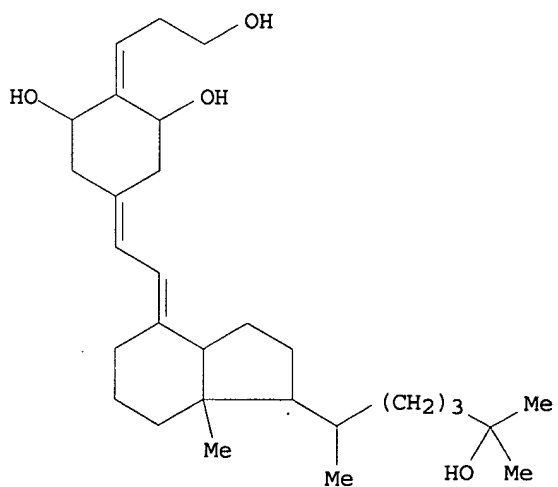


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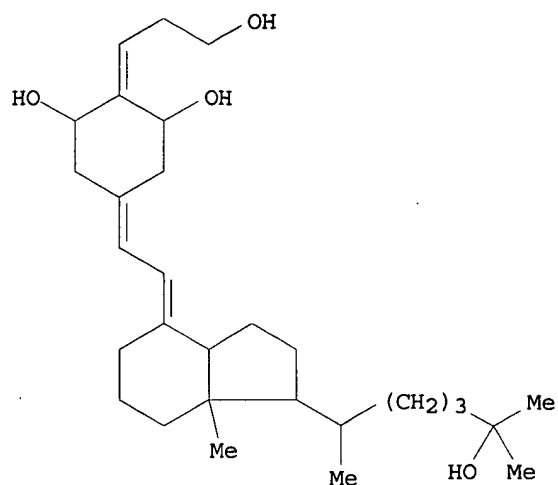
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2-(3-hydroxypropylidene)-, (1 α ,2E,3 β ,7E)- (9CI) (CA
INDEX NAME)



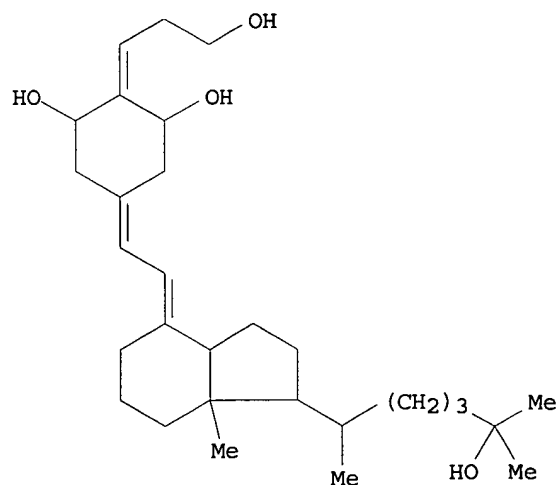
RN 781664-41-3 HCAPLUS
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 INDEX NAME)



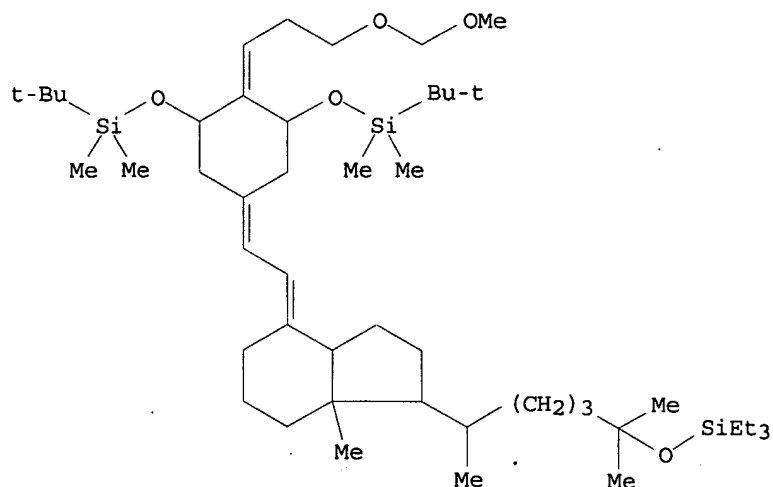
RN 781664-71-9 HCAPLUS
 CN 19-Nor-9,10-secocholesta-5,7-diene-1,3,25-triol,
 2-(3-hydroxypropylidene)-, (1 α ,2E,3 β ,7E,20S)- (9CI)
 (CA INDEX NAME)



RN 781664-72-0 HCAPLUS
 CN 19-Nor-9,10-secocholesta-5,7-diene-1,3,25-triol,
 2-(3-hydroxypropylidene)-, (1 α ,2Z,3 β ,7E,20S) - (9CI)
 (CA INDEX NAME)

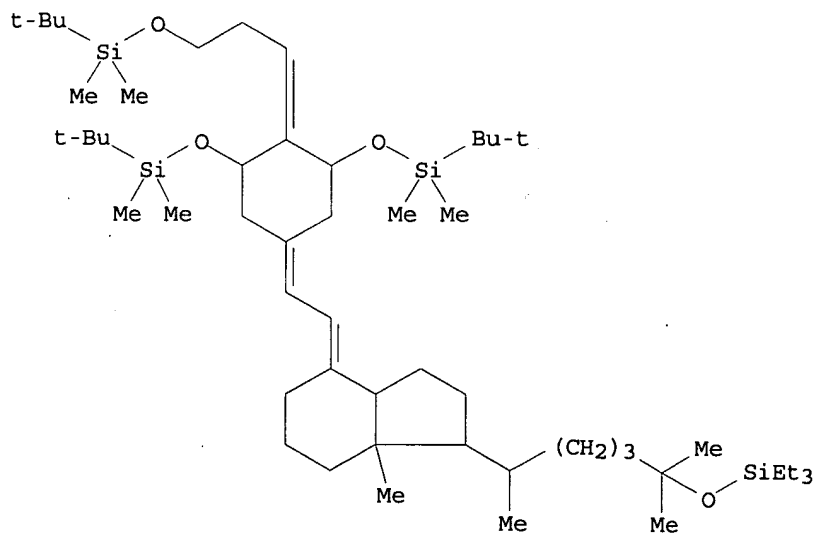


IT 766529-93-5P 781664-39-9P 781664-70-8P
 RL: RCT (Reactant); SPN (Synthetic preparation); PREP
 (Preparation); RACT (Reactant or reagent)
 (preparation of 2-propylidene-19-norvitaminD compds. as
 antiosteoporotics and antitumor agents)
 RN 766529-93-5 HCAPLUS
 CN Silane, [[(1 α ,3 β ,6E,7E)-2-[3-(methoxymethoxy)propylidene]-25-[(triethylsilyl)oxy]-19-nor-9,10-secocholesta-5,7,10(19)-triene-1,3-diyl]bis(oxy)]bis[(1,1-dimethylethyl)dimethyl- (9CI) (CA INDEX NAME)



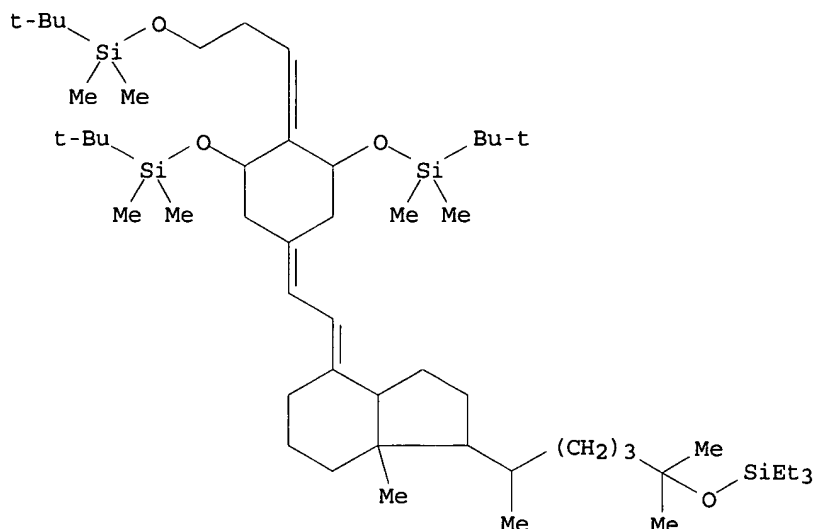
RN 781664-39-9 HCAPLUS

CN Silane, [[(1 α ,2E,3 β ,7E)-2-[3-[[[(1,1-dimethylethyl)dimethylsilyl]oxy]propylidene]-25-[(triethylsilyl)oxy]-19-nor-9,10-secocholesta-5,7-diene-1,3-diyl]bis(oxy)]bis[(1,1-dimethylethyl)dimethyl-(9CI) (CA INDEX NAME)



RN 781664-70-8 HCAPLUS

CN Silane, [[(1 α ,2E,3 β ,7E,20S)-2-[3-[[[(1,1-dimethylethyl)dimethylsilyl]oxy]propylidene]-25-[(triethylsilyl)oxy]-19-nor-9,10-secocholesta-5,7-diene-1,3-diyl]bis(oxy)]bis[(1,1-dimethylethyl)dimethyl-(9CI) (CA INDEX NAME)



IC ICM C07C401-00
 CC 32-7 (Steroids)
 Section cross-reference(s): 1, 63
 IT **766529-87-7P 781664-40-2P 781664-41-3P**
781664-71-9P 781664-72-0P
 RL: PAC (Pharmacological activity); SPN (Synthetic preparation);
 THU (Therapeutic use); BIOL (Biological study); PREP
 (Preparation); USES (Uses)

(preparation of 2-propylidene-19-norvitaminD compds. as
 antiosteoporotics and antitumor agents)

IT 78365-43-2P 120379-76-2P 163217-18-3P 194227-13-9P
 766529-88-8P 766529-89-9P 766529-90-2P 766529-91-3P
 766529-92-4P **766529-93-5P** 766529-94-6P 766529-95-7P
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 781664-43-5P 781664-44-6P **781664-70-8P**

RL: RCT (Reactant); SPN (Synthetic preparation); PREP
 (Preparation); RACT (Reactant or reagent)
 (preparation of 2-propylidene-19-norvitaminD compds. as
 antiosteoporotics and antitumor agents)

L17 ANSWER 4 OF 4 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2004:522163 HCAPLUS

DOCUMENT NUMBER: 141:314479

TITLE: New derivative of 1 α ,25-dihydroxy-19-norvitamin D3 with 3'-alkoxypropylidene moiety at C-2: synthesis, biological activity and conformational analysis

AUTHOR(S): Glebocka, Agnieszka; Sicinski, Rafal R.; DeLuca, Hector F.

CORPORATE SOURCE: Department of Biochemistry, University of Wisconsin-Madison, Madison, WI, 53706, USA

SOURCE: Journal of Steroid Biochemistry and Molecular Biology (2004), 89-90(1-5), 25-30
 CODEN: JSBBEZ; ISSN: 0960-0760

PUBLISHER: Elsevier Science Ltd.

DOCUMENT TYPE: Journal

LANGUAGE: English

OTHER SOURCE(S): CASREACT 141:314479

GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT
*

AB In pursuit of novel biol. active Vitamin D compds. of potential therapeutic value, $1\alpha,25$ -dihydroxy-2-[3'-(methoxymethoxy)propylidene]-19-norvitaminD3 (I) was efficiently prepared in a convergent synthesis, starting with (-)-quinic acid and the protected 25-hydroxy Grundmann ketone I. The key synthetic step involved Lythgoe type Wittig-Horner coupling of II, with the phosphine oxide III (R = SiCMe₃Me₂). Mol. modeling was employed to establish the A-ring conformation of the synthesized Vitamin I. Also, preliminary modeling of its complex with the rVDR was performed and interactions between ligand and the binding domain analyzed. Analog I was found to be only six times less potent than $1\alpha,25$ -(OH)₂D₃ in binding to the rat recombinant Vitamin D receptor (VDR). In comparison with hormone $1\alpha,25$ -(OH)₂D₃, it also showed slightly lower cellular HL-60-differentiation activity. Preliminary in vivo tests indicated unusually high calcemic activity of I.

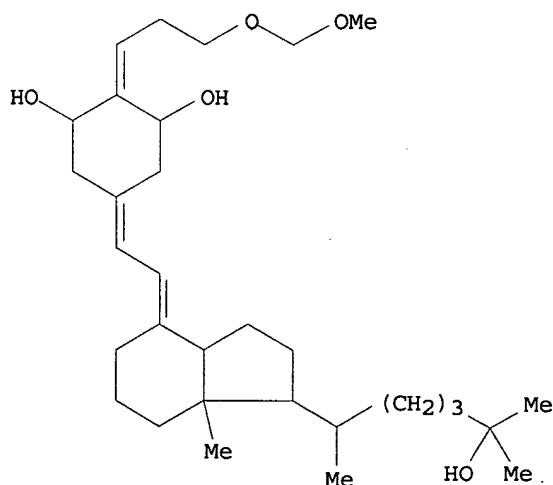
IT 766529-87-7P

RL: PAC (Pharmacological activity); PRP (Properties); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)

(preparation of a norvitamin D3 analog with 3'-alkoxypropylidene moiety at C-2 from (-)-quinic acid; its binding to the vitamin D receptor, and conformational anal.)

RN 766529-87-7 HCAPLUS

CN 19-Nor-9,10-secocholesta-5,7-diene-1,3,25-triol, 2-[3-(methoxymethoxy)propylidene]-, ($1\alpha,3\beta,6E,7E$)-(9CI) (CA INDEX NAME)



IT 766529-93-5P

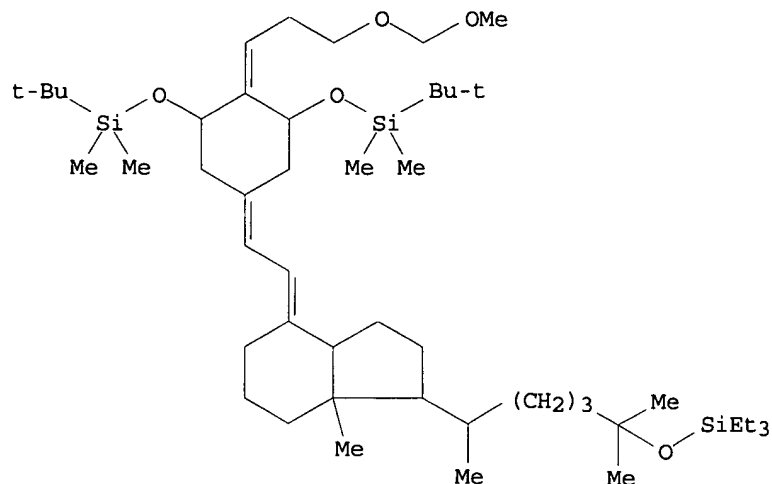
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(preparation of a norvitamin D3 analog with 3'-alkoxypropylidene moiety at C-2 from (-)-quinic acid; its binding to the vitamin D receptor, and conformational anal.)

RN 766529-93-5 HCAPLUS

CN Silane, [[($1\alpha,3\beta,6E,7E$)-2-[3-(methoxymethoxy)propylidene]-25-[(triethylsilyl)oxy]-19-nor-9,10-secocholesta-5,7,10(19)-triene-1,3-diyl]bis(oxy)]bis[(1,1-

dimethylethyl)dimethyl- (9CI) (CA INDEX NAME)



CC 32-7 (Steroids)

IT 766529-87-7P

RL: PAC (Pharmacological activity); PRP (Properties); SPN
(Synthetic preparation); BIOL (Biological study); PREP
(Preparation)

(preparation of a norvitamin D3 analog with 3'-alkoxypropylidene
moiety at C-2 from (-)-quinic acid; its binding to the vitamin
D receptor, and conformational anal.)

IT 665-27-0P 163217-18-3P 766529-88-8P 766529-89-9P
766529-90-2P 766529-91-3P 766529-92-4P 766529-93-5P
766529-94-6P 766529-95-7P 766529-96-8P 766529-97-9P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP
(Preparation); RACT (Reactant or reagent)

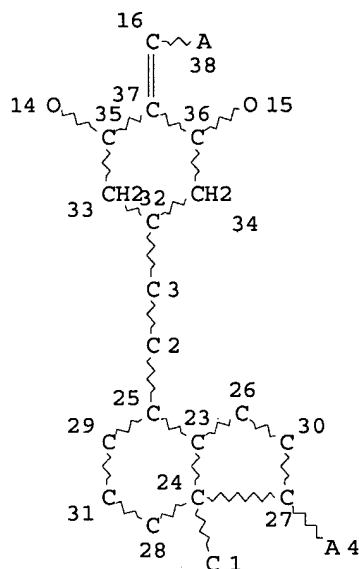
(preparation of a norvitamin D3 analog with 3'-alkoxypropylidene
moiety at C-2 from (-)-quinic acid; its binding to the vitamin
D receptor, and conformational anal.)

REFERENCE COUNT: 13 THERE ARE 13 CITED REFERENCES AVAILABLE
FOR THIS RECORD. ALL CITATIONS AVAILABLE
IN THE RE FORMAT

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L13 STR



NODE ATTRIBUTES:
 DEFAULT MLEVEL IS ATOM
 DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
 RING(S) ARE ISOLATED OR EMBEDDED
 NUMBER OF NODES IS 23

STEREO ATTRIBUTES: NONE

L15 50 SEA FILE=REGISTRY SSS FUL L13
 L16 8 SEA FILE=REGISTRY ABB=ON PLU=ON L15 AND L2
 L17 4 SEA FILE=HCAPLUS ABB=ON PLU=ON L16
 L18 10 SEA FILE=HCAPLUS ABB=ON PLU=ON L15
 L19 6 SEA FILE=HCAPLUS ABB=ON PLU=ON L18 NOT L17

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L19 ANSWER 1 OF 6 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2006:505971 HCAPLUS

DOCUMENT NUMBER: 145:201953

TITLE: Analogs of 1 α ,25-dihydroxyvitamin D3
 with high potency in induction of
 osteoclastogenesis and prevention of dendritic
 cell differentiation: Synthesis and biological
 evaluation of 2-substituted 19-norvitamin D
 analogs

AUTHOR(S): Shimazaki, Mika; Miyamoto, Yukiko; Yamamoto,
 Keiko; Yamada, Sachiko; Takami, Masamichi;
 Shinki, Toshimasa; Udagawa, Nobuyuki; Shimizu,
 Masato

CORPORATE SOURCE: Institute of Biomaterials and Bioengineering
 Tokyo Medical and Dental University,
 Chiyoda-ku, Tokyo, 101-0062, Japan

SOURCE: Bioorganic & Medicinal Chemistry (2006),
 14(13), 4645-4656

CODEN: BMECEP; ISSN: 0968-0896

PUBLISHER: Elsevier B.V.

DOCUMENT TYPE: Journal

LANGUAGE: English

AB In our previous papers, we found that introduction of a

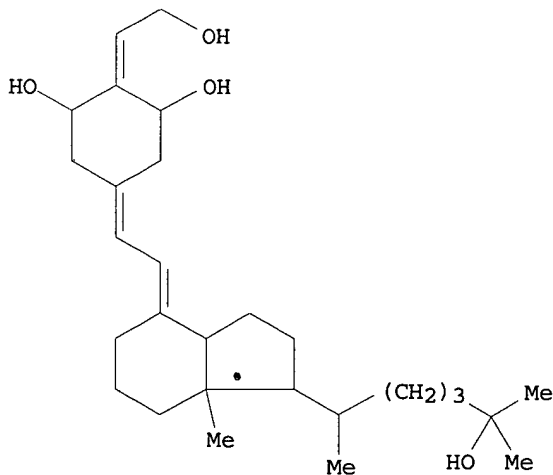
substituent at C(2) into 1 α ,25-dihydroxy-19-norvitaminD3 (2a) caused dramatic changes in binding affinity for the vitamin D receptor (VDR) and in transcriptional activity compared with the parent compound. To investigate the broad biol. activity of 2-substituted 19-norvitamin D analogs, we synthesized two new (20S)-2-hydroxyethylidene-19-norvitaminD derivs. (3b and 4b) and a total of 16 A-ring-modified analogs including 3b and 4b were tested for the following in vitro and in vivo biol. activities: (1) affinity for the VDR, (2) transcriptional activity, (3) osteoclast formation, (4) bone calcium mobilization in rats, and (5) effects on differentiation of dendritic cells (DCs). The biol. effects of the analogs were compared with those of 1 α ,25-dihydroxyvitamin D3 (1a) and 2MD, which is being developed for the treatment of osteoporosis. The efficacy of the (20S)-19-norvitamin D analogs with 2-hydroxyethylidene, 2-hydroxyethoxy, and 2-Me moieties (3b, 5b, 6b, and 9b) was more than 10-fold stronger than that of 1a with respect to transcriptional activity, ability to induce osteoclast formation, and ability to inhibit CD86 expression, a marker of mature DCs, and was similar to that of 2MD. The (20S)-2 β -hydroxyethoxy derivative 6b was 2 orders of magnitude more active than 1a and approx. twice as potent as 2MD in preventing CD86 production. The 2-epoxy derivs. 7 and 8 were relatively poor ligands for the VDR and exhibited activity lower than that of the natural hormone 1a.

IT 681830-60-4P 681830-61-5P

RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(dihydroxyvitamin D3 analogs with potency in induction of osteoclastogenesis and prevention of dendritic cell differentiation)

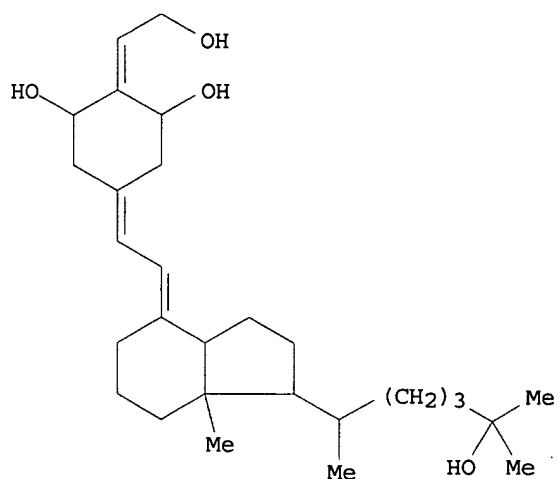
RN 681830-60-4 HCAPLUS

CN 19-Nor-9,10-secocholesta-5,7-diene-1,3,25-triol,
2-(2-hydroxyethylidene)-, (1 α ,2E,3 β ,7E,20S)- (9CI) (CA
INDEX NAME)



RN 681830-61-5 HCAPLUS

CN 19-Nor-9,10-secocholesta-5,7-diene-1,3,25-triol,
2-(2-hydroxyethylidene)-, (1 α ,2Z,3 β ,7E,20S)- (9CI) (CA
INDEX NAME)



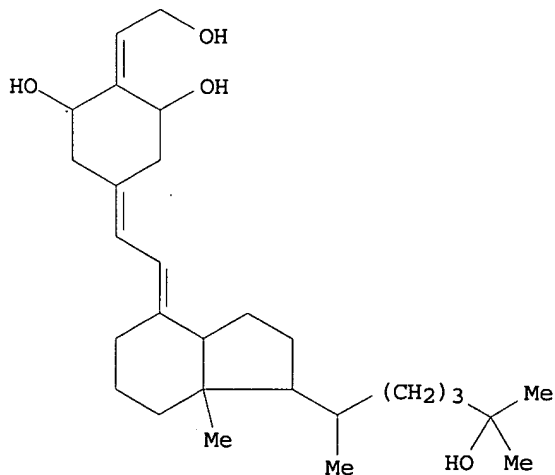
IT 737757-31-2 897923-11-4

RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(dihydroxyvitamin D3 analogs with potency in induction of osteoclastogenesis and prevention of dendritic cell differentiation)

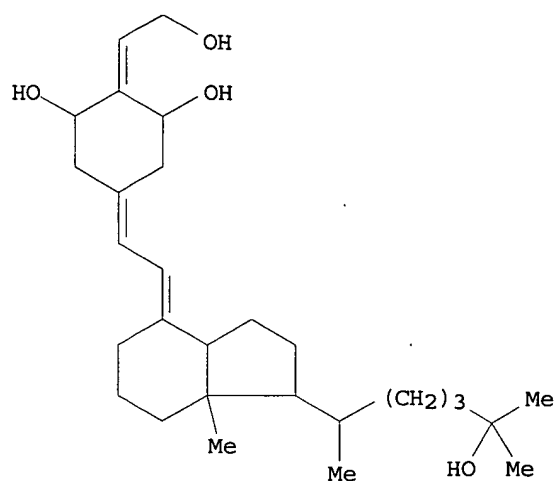
RN 737757-31-2 HCAPLUS

CN 19-Nor-9,10-secocholesta-5,7-diene-1,3,25-triol, 2-(2-hydroxyethylidene)-, (1 α ,2Z,3 β ,7E)- (9CI) (CA INDEX NAME)



RN 897923-11-4 HCAPLUS

CN 1,3-Cyclohexanediol, 2-(2-hydroxyethylidene)-5-[[[(1S,3aS,7aS)-octahydro-1-[(1S)-5-hydroxy-1,5-dimethylhexyl]-7a-methyl-4H-inden-4-ylidene]ethylidene]-, (1R,2S,3R)- (9CI) (CA INDEX NAME)

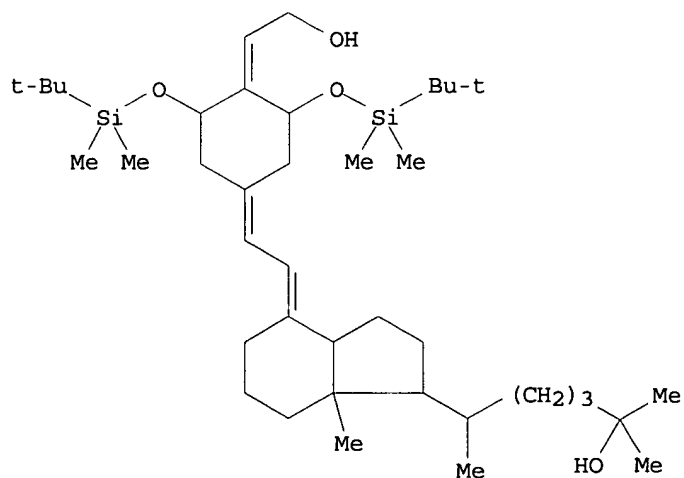


IT 681831-02-7P 681856-69-9P 900181-62-6P
900181-63-7P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP
(Preparation); RACT (Reactant or reagent)
(dihydroxyvitamin D3 analogs with potency in induction of
osteoclastogenesis and prevention of dendritic cell
differentiation)

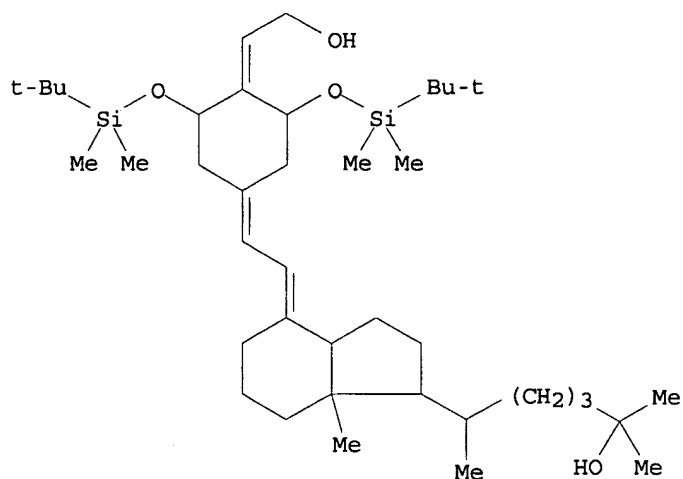
RN 681831-02-7 HCAPLUS

CN 19-Nor-9,10-secocholesta-5,7-dien-25-ol,1,3-bis[[(1,1-
dimethylethyl)dimethylsilyl]oxy]-2-(2-hydroxyethylidene)-,
(1α,2E,3β,7E,20S)- (9CI) (CA INDEX NAME)



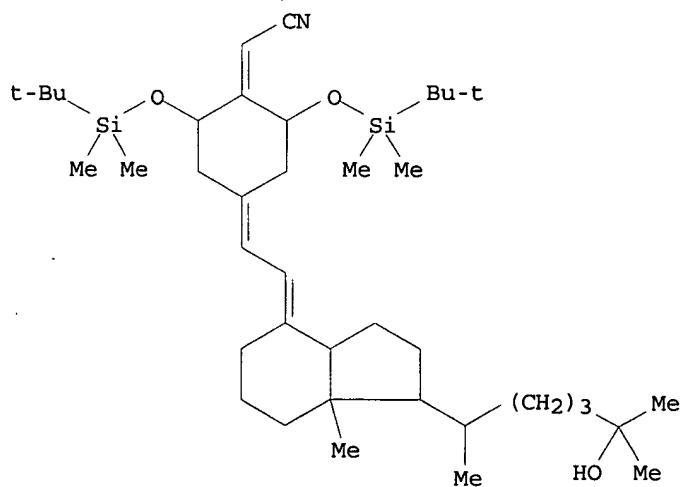
RN 681856-69-9 HCAPLUS

CN 19-Nor-9,10-secocholesta-5,7-dien-25-ol,1,3-bis[[(1,1-
dimethylethyl)dimethylsilyl]oxy]-2-(hydroxyethylidene)-,
(1α,2Z,3β,7E,20S)- (9CI) (CA INDEX NAME)



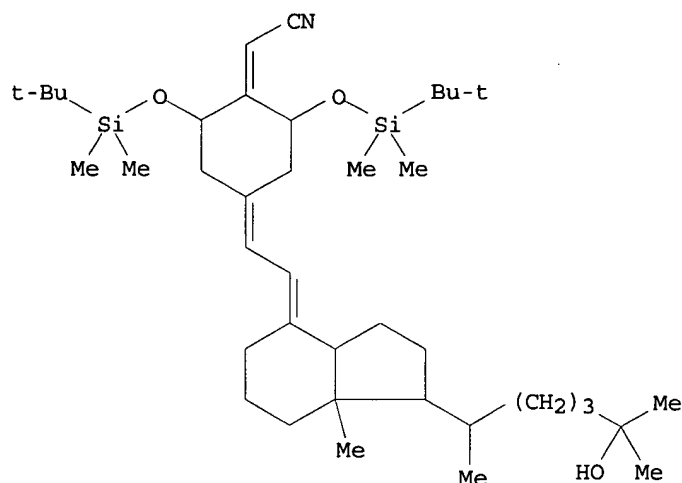
RN 900181-62-6 HCAPLUS

CN Acetonitrile, [(1 α ,3 β ,7E,20S)-1,3-bis[[[(1,1-dimethylethyl)dimethylsilyl]oxy]-25-hydroxy-19-nor-9,10-secocholesta-5,7-dien-2-ylidene]-, (2E)- (9CI) (CA INDEX NAME)



RN 900181-63-7 HCAPLUS

CN Acetonitrile, [(1 α ,3 β ,7E,20S)-1,3-bis[[[(1,1-dimethylethyl)dimethylsilyl]oxy]-25-hydroxy-19-nor-9,10-secocholesta-5,7-dien-2-ylidene]-, (2Z)- (9CI) (CA INDEX NAME)



CC 1-3 (Pharmacology)
 Section cross-reference(s): 2, 32

IT **681830-60-4P 681830-61-5P**
 RL: PAC (Pharmacological activity); SPN (Synthetic preparation);
 THU (Therapeutic use); BIOL (Biological study); PREP
 (Preparation); USES (Uses)
 (dihydroxyvitamin D3 analogs with potency in induction of
 osteoclastogenesis and prevention of dendritic cell
 differentiation)

IT 32222-06-3 130447-37-9 134523-84-5 195051-26-4 546095-46-9
 546100-84-9 681433-59-0 681830-46-6 681830-47-7
 681830-58-0 681830-59-1 681830-95-5 681830-96-6
 681856-65-5 **737757-31-2** 849816-81-5 849915-28-2
897923-11-4
 RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL
 (Biological study); USES (Uses)
 (dihydroxyvitamin D3 analogs with potency in induction of
 osteoclastogenesis and prevention of dendritic cell
 differentiation)

IT 681433-76-1P 681830-99-9P 681831-00-5P **681831-02-7P**
681856-69-9P 681857-03-4P **900181-62-6P**
900181-63-7P 903900-67-4P
 RL: RCT (Reactant); SPN (Synthetic preparation); PREP
 (Preparation); RACT (Reactant or reagent)
 (dihydroxyvitamin D3 analogs with potency in induction of
 osteoclastogenesis and prevention of dendritic cell
 differentiation)

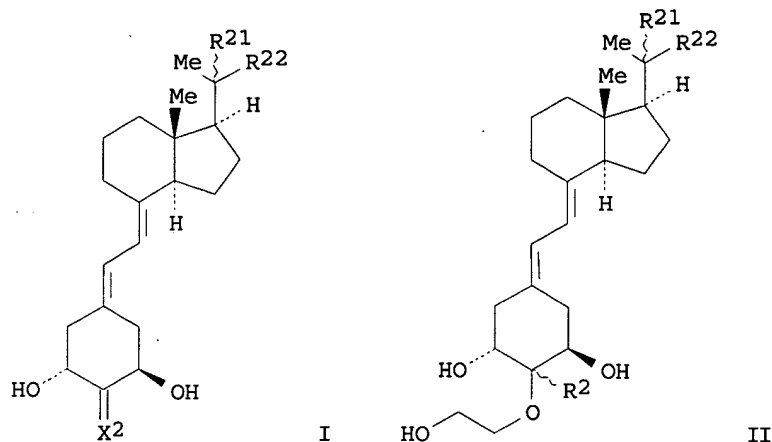
REFERENCE COUNT: 41 THERE ARE 41 CITED REFERENCES AVAILABLE
 FOR THIS RECORD. ALL CITATIONS AVAILABLE
 IN THE RE FORMAT

L19 ANSWER 2 OF 6 HCAPLUS COPYRIGHT 2006 ACS on STN
 ACCESSION NUMBER: 2006:447143 HCAPLUS
 DOCUMENT NUMBER: 145:124780
 TITLE: Synthesis and biological activities of new
 1 α ,25-dihydroxy-19-norvitamin D3 analogs
 with modifications in both the A-ring and the
 side chain

AUTHOR(S): Shimizu, Masato; Miyamoto, Yukiko; Kobayashi,
 Emi; Shimazaki, Mika; Yamamoto, Keiko;
 Reischl, Wolfgang; Yamada, Sachiko

CORPORATE SOURCE: Laboratory of Medicinal Chemistry, School of
 Biomedical Science, Tokyo Medical and Dental
 University, 2-3-10 Kandasurugadai, Chiyoda-ku,

SOURCE: Tokyo, 101-0062, Japan
 Bioorganic & Medicinal Chemistry (2006),
 14(12), 4277-4294
 CODEN: BMECEP; ISSN: 0968-0896
 PUBLISHER: Elsevier B.V.
 DOCUMENT TYPE: Journal
 LANGUAGE: English
 OTHER SOURCE(S): CASREACT 145:124780
 GI



AB In a series of studies on structure-activity relationships of 2-substituted 19-norvitamin D analogs, we found that 1 α ,25-dihydroxy-19-norvitamin D3 analogs with 2 β -hydroxyethoxy or 2E-hydroxyethylidene moieties show strong binding affinity for the vitamin D receptor (VDR) as well as marked transcriptional activity. To further examine the effects of side chain structure on the activity of 2-substituted 19-norvitamin D analogs, we have synthesized new 19-norvitamin D3 analogs with modifications in both the A-ring at the C(2) position and the side chain. The side chains of these analogs contained a double bond between C(22) and C(23) or an oxygen atom at C(22). The biol. activity of the analogs was evaluated in vitro. All the side chain-modified analogs were less active than 1 α ,25-dihydroxyvitamin D3 and the parent compds. I [X2 = CHCH2OH-(E), -(Z), R21 = β -H, R22 = (CH2)3CMe2OH] and II [R2 = α -, β -H, R21 = β -H, R22 = (CH2)3CMe2OH] possessing a natural 20R-configuration in binding to the VDR, but, except for the (20R)-22-oxa analogs I [X2 = CHCH2OH-(E), -(Z), R21 = α -H, R22 = O(CH2)2CMe2OH] and II [R2 = α -, β -H, R21 = α -H, R22 = O(CH2)2CMe2OH], were significantly more potent in transcriptional activity. Of the side-chain-modified analogs the 2 β -hydroxyethoxy- and 2E-hydroxyethylidene-22,24-diene-24a,26a,27a-trihomo analogs showed markedly higher transcriptional activity (25- and 17.5-fold, resp.) compared with 1 α ,25-dihydroxyvitamin D3. Elongation of the side chain at the C-24, C-26, and C-27 positions and introduction of a 22,24-diene moiety strongly increased transcriptional activity, as seen in the 20-epi analogs I [X2 = CHCH2OH-(E), -(Z), R21 = α -H, R22 = (CH2)3CMe2OH] and II [R2 = α -, β -H, R21 = α -H, R22 = (CH2)3CMe2OH].

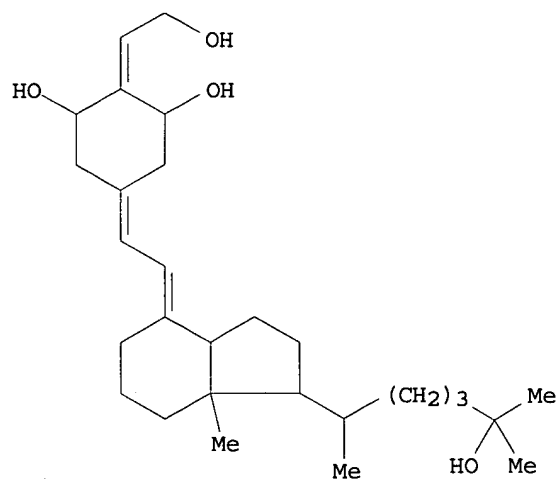
IT 681830-60-4 681830-61-5 737757-31-2
 897923-11-4

RL: PAC (Pharmacological activity); BIOL (Biological study)

(synthesis and vitamin D receptor binding activity of new
1 α ,25-dihydroxy-19-norvitaminD3 analogs with
modifications in both the A-ring and the side chain)

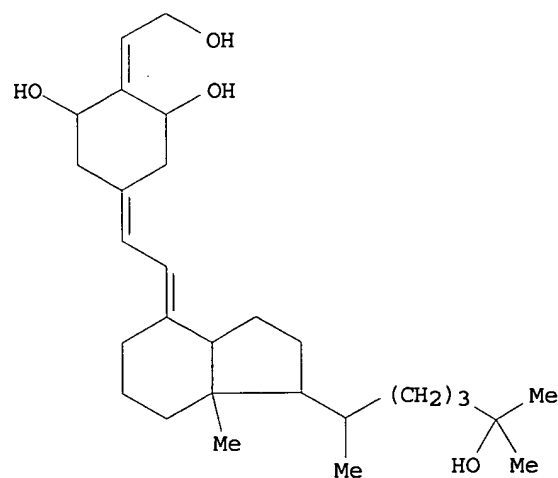
RN 681830-60-4 HCAPLUS

CN 19-Nor-9,10-secocholesta-5,7-diene-1,3,25-triol,
2-(2-hydroxyethylidene)-, (1 α ,2E,3 β ,7E,20S)- (9CI) (CA
INDEX NAME)



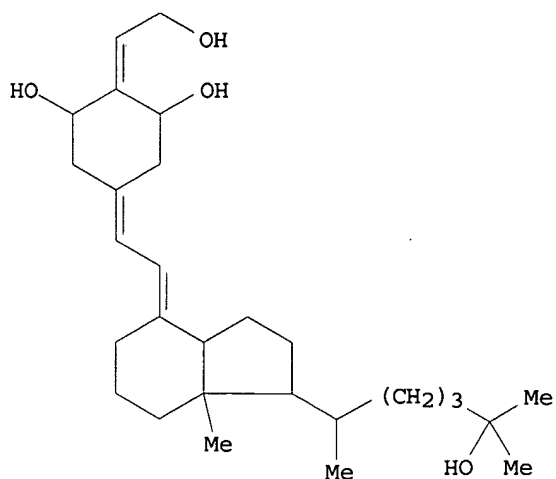
RN 681830-61-5 HCAPLUS

CN 19-Nor-9,10-secocholesta-5,7-diene-1,3,25-triol,
2-(2-hydroxyethylidene)-, (1 α ,2Z,3 β ,7E,20S)- (9CI) (CA
INDEX NAME)



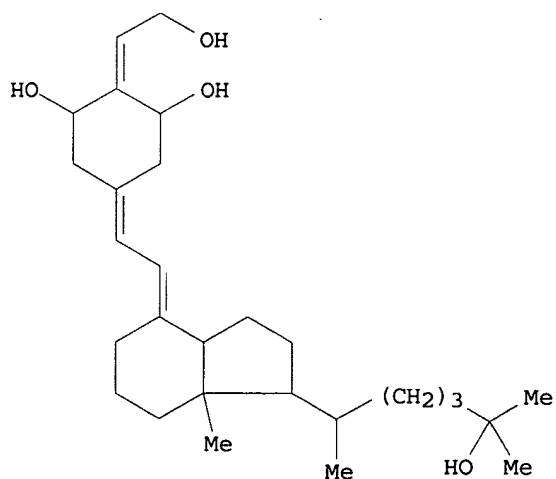
RN 737757-31-2 HCAPLUS

CN 19-Nor-9,10-secocholesta-5,7-diene-1,3,25-triol,
2-(2-hydroxyethylidene)-, (1 α ,2Z,3 β ,7E)- (9CI) (CA
INDEX NAME)



RN 897923-11-4 HCAPLUS

CN 1,3-Cyclohexanediol, 2-(2-hydroxyethylidene)-5-[[[(1S,3aS,7aS)-octahydro-1-[(1S)-5-hydroxy-1,5-dimethylhexyl]-7a-methyl-4H-inden-4-ylidene]ethylidene]-, (1R,2S,3R)-(9CI) (CA INDEX NAME)



IT 681830-66-0P 681830-67-1P 681830-74-0P

681830-75-1P 681830-84-2P 681830-85-3P

897923-07-8P 897923-08-9P

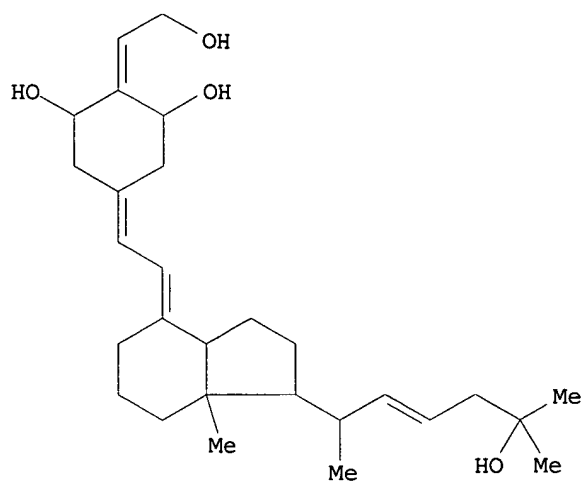
RL: PAC (Pharmacological activity); SPN (Synthetic preparation);

BIOL (Biological study); PREP (Preparation)

(synthesis and vitamin D receptor binding activity of new
1α,25-dihydroxy-19-norvitamin D3 analogs with
modifications in both the A-ring and the side chain)

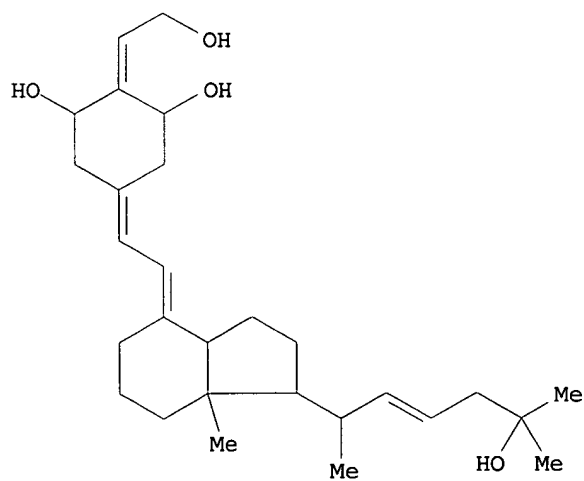
RN 681830-66-0 HCAPLUS

CN 19-Nor-9,10-secocholesta-5,7,22-triene-1,3,25-triol,
2-(2-hydroxyethylidene)-, (1α,2E,3β,7E,22E)-(9CI) (CA
INDEX NAME)



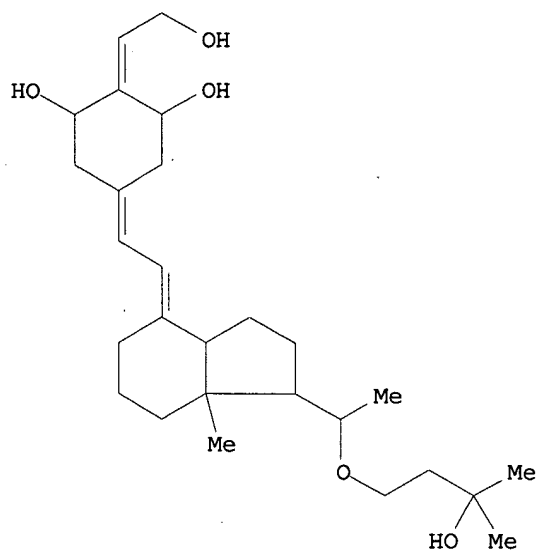
RN 681830-67-1 HCAPLUS

CN 19-Nor-9,10-secocholesta-5,7,22-triene-1,3,25-triol,
2-(2-hydroxyethylidene)-, (1 α ,2Z,3 β ,7E,22E)- (9CI) (CA
INDEX NAME)



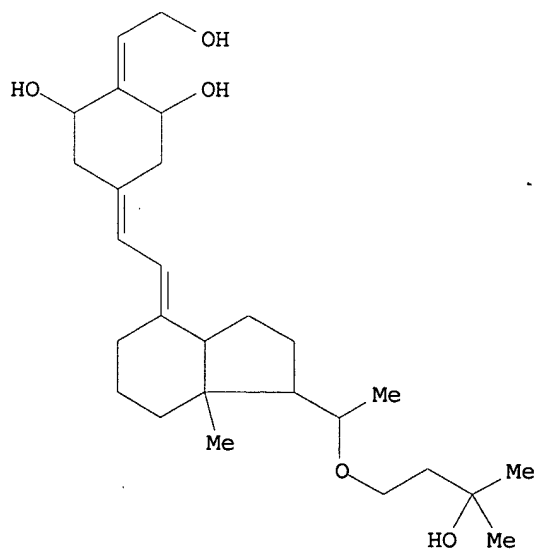
RN 681830-74-0 HCAPLUS

CN 1,3-Cyclohexanediol, 2-(2-hydroxyethylidene)-5-[[octahydro-1-[1-(3-
hydroxy-3-methylbutoxy)ethyl]-7a-methyl-4H-inden-4-
ylidene]ethylidene]-, stereoisomer (9CI) (CA INDEX NAME)



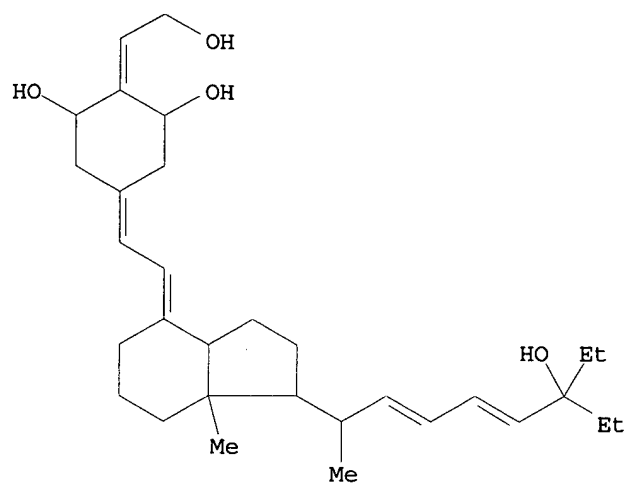
RN 681830-75-1 HCAPLUS

CN 1,3-Cyclohexanediol, 2-(2-hydroxyethylidene)-5-[[octahydro-1-[1-(3-hydroxy-3-methylbutoxy)ethyl]-7a-methyl-4H-inden-4-ylidene]ethylidene]-, stereoisomer (9CI) (CA INDEX NAME)



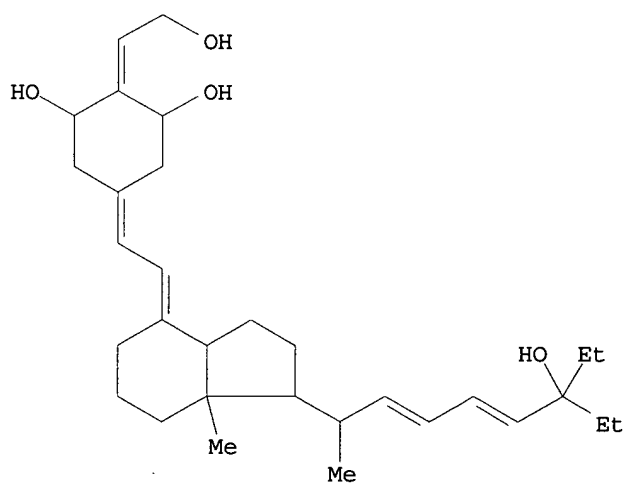
RN 681830-84-2 HCAPLUS

CN 1,3-Cyclohexanediol, 5-[[1-(6-ethyl-6-hydroxy-1-methyl-2,4-octadienyl)octahydro-7a-methyl-4H-inden-4-ylidene]ethylidene]-2-(2-hydroxyethylidene)-, stereoisomer (9CI) (CA INDEX NAME)



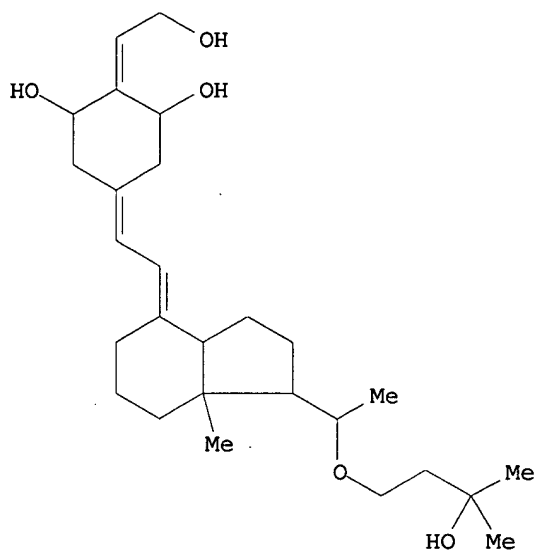
RN 681830-85-3 HCAPLUS

CN 1,3-Cyclohexanediol, 5-[[1-(6-ethyl-6-hydroxy-1-methyl-2,4-octadienyl)octahydro-7a-methyl-4H-inden-4-ylidene]ethylidene]-2-(2-hydroxyethylidene)-, stereoisomer (9CI) (CA INDEX NAME)



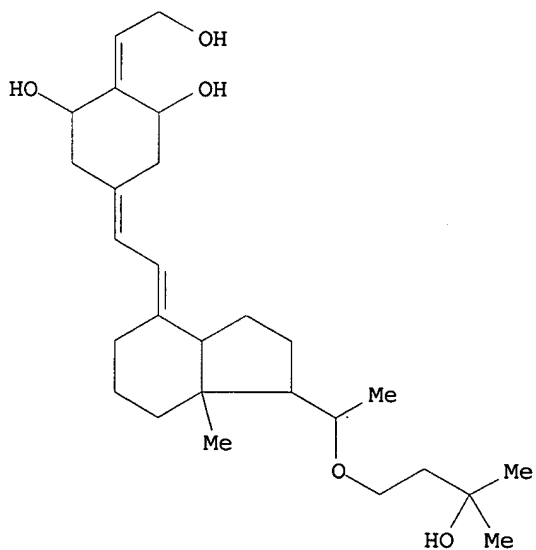
RN 897923-07-8 HCAPLUS

CN 1,3-Cyclohexanediol, 2-(2-hydroxyethylidene)-5-[(2E)-[(1S,3aS,7aS)-octahydro-1-[(1S)-1-(3-hydroxy-3-methylbutoxy)ethyl]-7a-methyl-4H-inden-4-ylidene]ethylidene]-, (1R,2E,3R)- (9CI) (CA INDEX NAME)



RN 897923-08-9 HCAPLUS

CN 1,3-Cyclohexanediol, 2-(2-hydroxyethylidene)-5-[(2E)-[(1S,3aS,7aS)-octahydro-1-[(1S)-1-(3-hydroxy-3-methylbutoxy)ethyl]-7a-methyl-4H-inden-4-ylidene]ethylidene]-, (1R,2Z,3R)- (9CI) (CA INDEX NAME)



IT 681434-05-9P 681434-06-0P 681434-13-9P
681434-14-0P 681831-07-2P 681831-08-3P
681831-10-7P 681856-70-2P 681856-71-3P
897657-90-8P 897657-91-9P 897657-92-0P

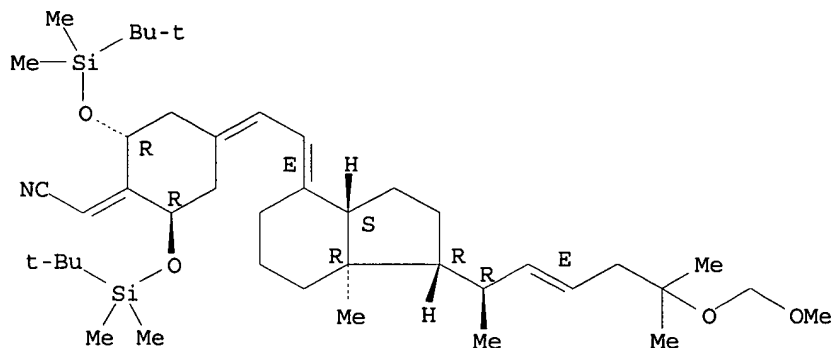
RL: RCT (Reactant); SPN (Synthetic preparation); PREP
(Preparation); RACT (Reactant or reagent)
(synthesis and vitamin D receptor binding activity of new
1 α ,25-dihydroxy-19-norvitamin D3 analogs with
modifications in both the A-ring and the side chain)

RN 681434-05-9 HCAPLUS

CN Acetonitrile, [(2R,6R)-2,6-bis[[[(1,1-dimethylethyl)dimethylsilyl]oxy]-4-[(2E)-[(1R,3aS,7aR)-octahydro-1-[(1R,2E)-5-(methoxymethoxy)-1,5-dimethyl-2-hexenyl]-7a-methyl-4H-inden-4-

ylidene]ethylidene]cyclohexylidene] - (9CI) (CA INDEX NAME)

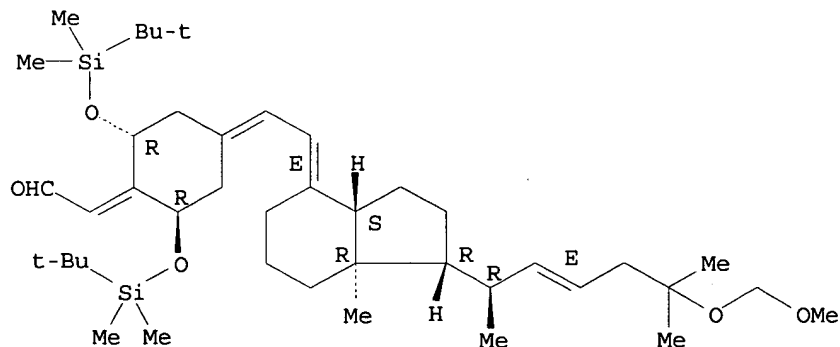
Absolute stereochemistry.
Double bond geometry as shown.



RN 681434-06-0 HCAPLUS

CN Acetaldehyde, [(2R,6R)-2,6-bis[[[(1,1-dimethylethyl)dimethylsilyl]oxy]-4-[(2E)-[(1R,3aS,7aR)-octahydro-1-[(1R,2E)-5-(methoxymethoxy)-1,5-dimethyl-2-hexenyl]-7a-methyl-4H-inden-4-ylidene]ethylidene]cyclohexylidene] - (9CI) (CA INDEX NAME)

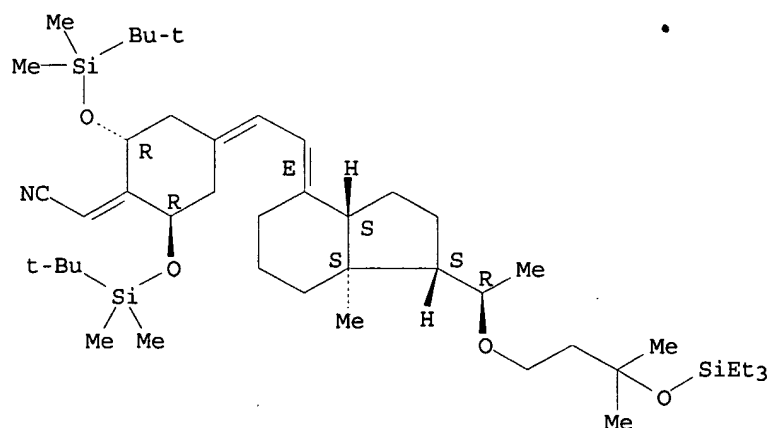
Absolute stereochemistry.
Double bond geometry as shown.



RN 681434-13-9 HCAPLUS

CN Acetonitrile, [(2R,6R)-2,6-bis[[[(1,1-dimethylethyl)dimethylsilyl]oxy]-4-[(2E)-[(1S,3aS,7aS)-octahydro-7a-methyl-1-[(1R)-1-[3-methyl-3-[(triethylsilyl)oxy]butoxy]ethyl]-4H-inden-4-ylidene]ethylidene]cyclohexylidene] - (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.

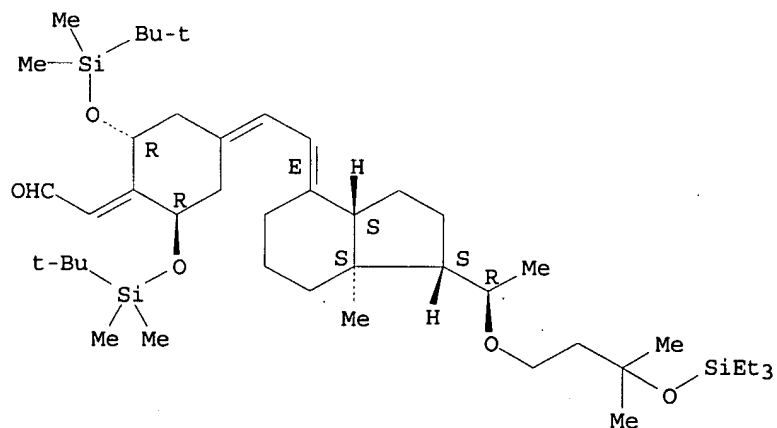


RN 681434-14-0 HCAPLUS

CN Acetaldehyde, [(2R,6R)-2,6-bis[[[(1,1-dimethylethyl)dimethylsilyl]oxy]-4-[(2E)-[(1S,3aS,7aS)-octahydro-7a-methyl-1-[(1R)-1-[3-methyl-3-[(triethylsilyl)oxy]butoxy]ethyl]-4H-inden-4-ylidene]ethylidene]cyclohexylidene]-(9CI) (CA INDEX NAME)

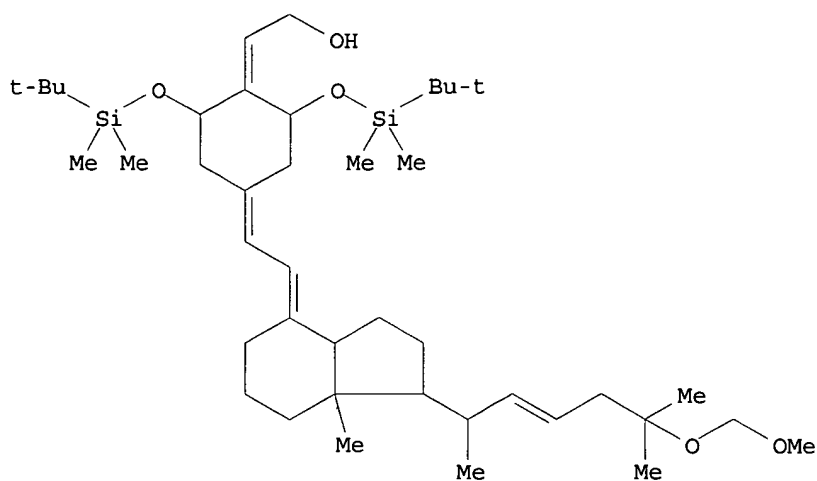
Absolute stereochemistry.

Double bond geometry as shown.



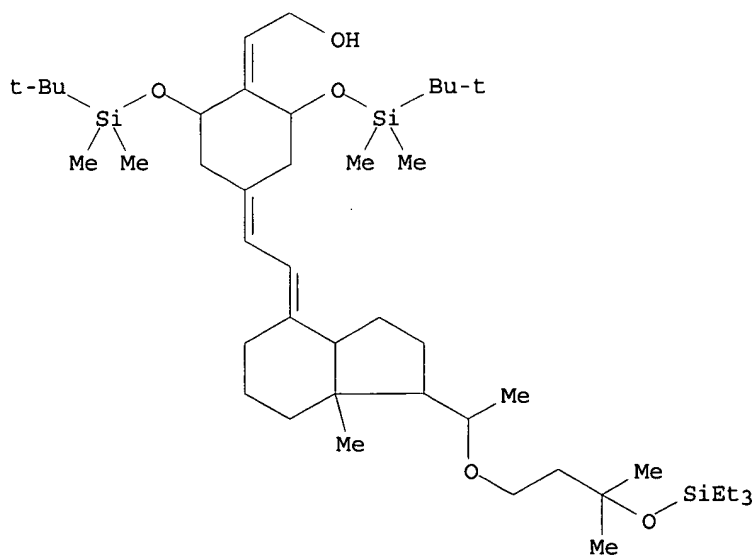
RN 681831-07-2 HCAPLUS

CN Ethanol, 2-[(1 α ,3 β ,7E,22E)-1,3-bis[[[(1,1-dimethylethyl)dimethylsilyl]oxy]-25-(methoxymethoxy)-19-nor-9,10-secocholesta-5,7,22-trien-2-ylidene]-, (2E)- (9CI) (CA INDEX NAME)



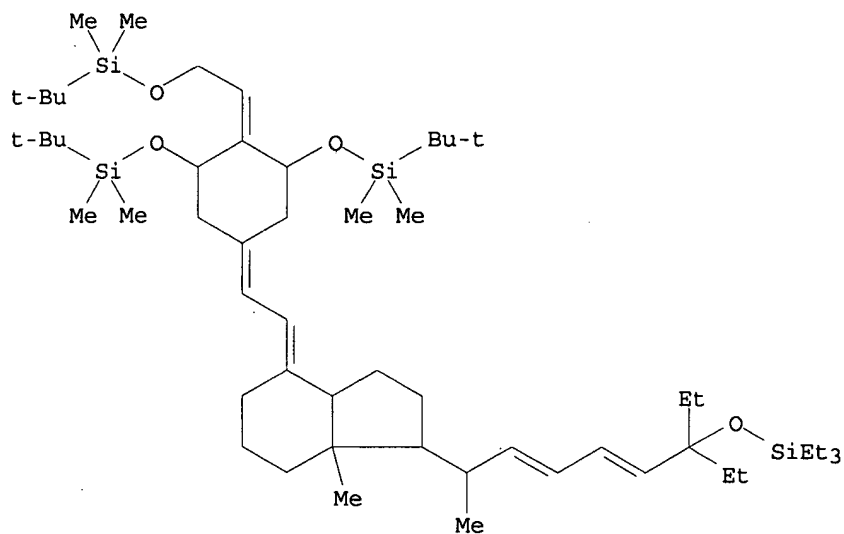
RN 681831-08-3 HCAPLUS

CN Ethanol, 2-[2,6-bis[[1,1-dimethylethyl]dimethylsilyl]oxy]-4-
 [[octahydro-7a-methyl-1-[1-[3-methyl-3-
 [(triethylsilyl)oxy]butoxy]ethyl]-4H-inden-4-
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 INDEX NAME)



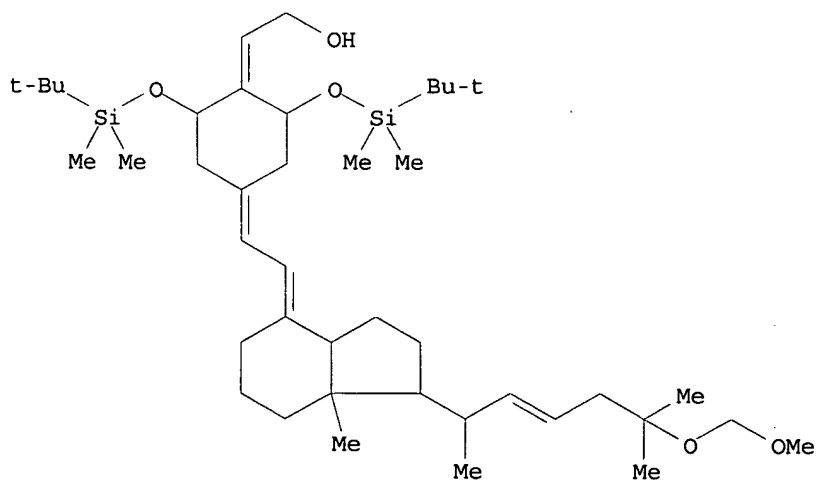
RN 681831-10-7 HCAPLUS

CN Silane, [[(1R,3R)-2-[(1E)-2-[[1,1-dimethylethyl]dimethylsilyl]oxy
]ethylidene]-5-[(2E)-[(1R,3aS,7aR)-1-[(1R,2E,4E)-6-ethyl-1-methyl-
 6-[(triethylsilyl)oxy]-2,4-octadienyl]octahydro-7a-methyl-4H-inden-
 4-ylidene]ethylidene]-1,3-cyclohexanediyl]bis(oxy)]bis[(1,1-
 dimethylethyl)dimethyl]- (9CI) (CA INDEX NAME)



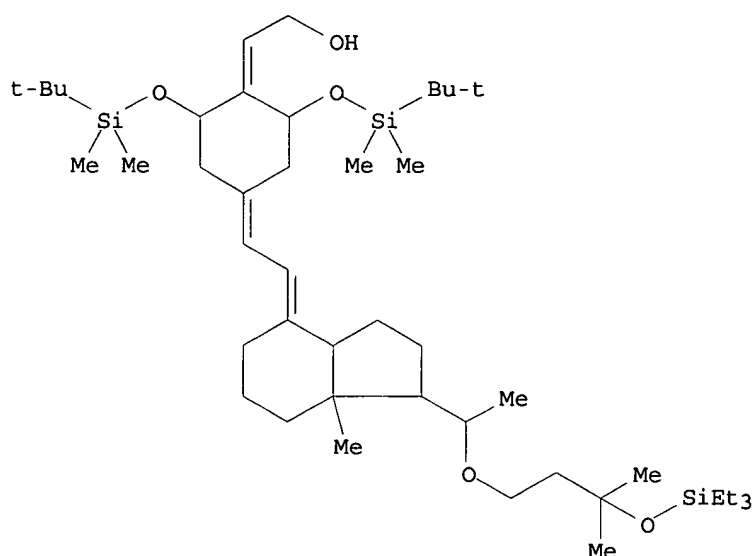
RN 681856-70-2 HCAPLUS

CN Ethanol, 2-[(1 α ,3 β ,7E,22E)-1,3-bis[[(1,1-dimethylethyl)dimethylsilyl]oxy]-25-(methoxymethoxy)-19-nor-9,10-secocholesta-5,7,22-trien-2-ylidene]-, (2Z)- (9CI) (CA INDEX NAME)



RN 681856-71-3 HCAPLUS

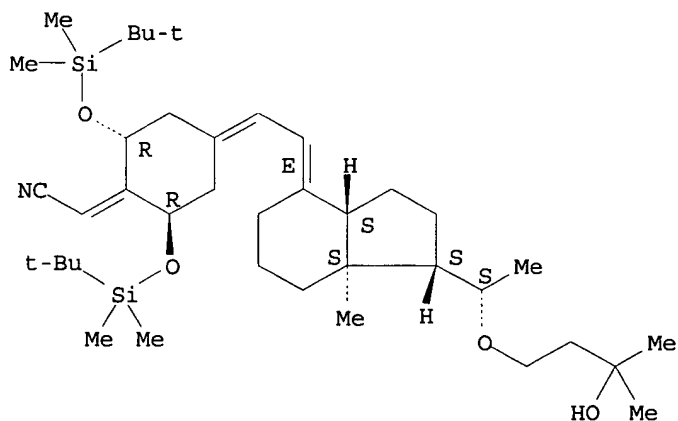
CN Ethanol, 2-[2,6-bis[[(1,1-dimethylethyl)dimethylsilyl]oxy]-4-[[octahydro-7a-methyl-1-[1-[3-methyl-3-[(triethylsilyl)oxy]butoxy]ethyl]-4H-inden-4-ylidene]ethylidene]cyclohexylidene]-, stereoisomer (9CI) (CA INDEX NAME)



RN 897657-90-8 HCAPLUS

CN Acetonitrile, [(2R,6R)-2,6-bis[[[(1,1-dimethylethyl)dimethylsilyl]oxy]-4-[(2E)-[(1S,3aS,7aS)-octahydro-1-[(1S)-1-(3-hydroxy-3-methylbutoxy)ethyl]-7a-methyl-4H-inden-4-ylidene]ethylidene]cyclohexylidene]-(9CI) (CA INDEX NAME)

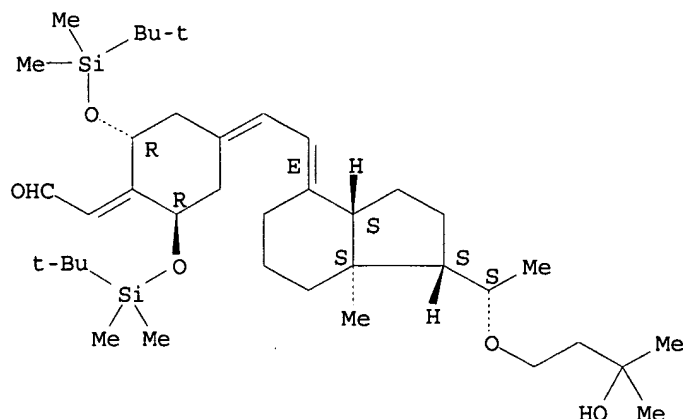
Absolute stereochemistry.
Double bond geometry as shown.



RN 897657-91-9 HCAPLUS

CN Acetaldehyde, [(2R,6R)-2,6-bis[[[(1,1-dimethylethyl)dimethylsilyl]oxy]-4-[(2E)-[(1S,3aS,7aS)-octahydro-1-[(1S)-1-(3-hydroxy-3-methylbutoxy)ethyl]-7a-methyl-4H-inden-4-ylidene]ethylidene]cyclohexylidene]-(9CI) (CA INDEX NAME)

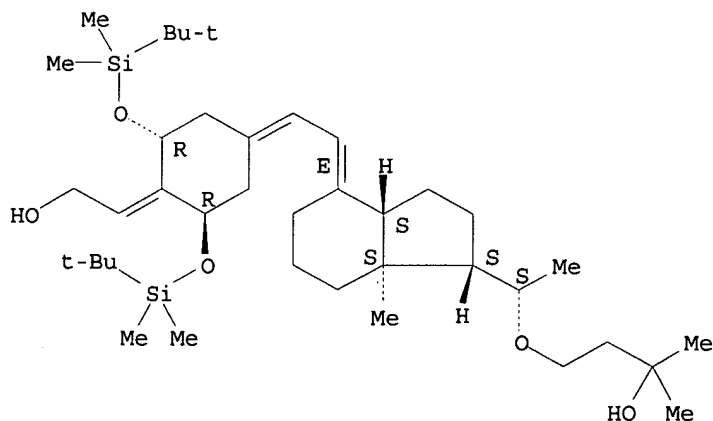
Absolute stereochemistry.
Double bond geometry as shown.



RN 897657-92-0 HCAPLUS

CN 2-Butanol, 4-[(1S)-1-[(1S,3aS,4E,7aS)-4-[[[(3R,5R)-3,5-bis[[[(1,1-dimethylethyl)dimethylsilyl]oxy]-4-(2-hydroxyethylidene)cyclohexylidene]ethylidene]octahydro-7a-methyl-1H-inden-1-yl]ethoxy]-2-methyl-(9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



CC 32-7 (Steroids)

Section cross-reference(s): 1

IT 32222-06-3, 1 α ,25-Dihydroxyvitamin D3 546095-46-9

546100-84-9 681830-58-0 681830-59-1 681830-60-4

681830-61-5 737757-31-2 897923-11-4

RL: PAC (Pharmacological activity); BIOL (Biological study)

(synthesis and vitamin D receptor binding activity of new 1 α ,25-dihydroxy-19-norvitamin D3 analogs with modifications in both the A-ring and the side chain)

IT 67-97-ODP, Cholecalciferol, analogs 681830-64-8P 681830-65-9P

681830-66-0P 681830-67-1P 681830-72-8P

681830-73-9P 681830-74-0P 681830-75-1P

681830-82-0P 681830-83-1P 681830-84-2P

681830-85-3P 897923-07-8P 897923-08-9P

897923-09-0P 897923-10-3P

RL: PAC (Pharmacological activity); SPN (Synthetic preparation);

BIOL (Biological study); PREP (Preparation)

(synthesis and vitamin D receptor binding activity of new 1 α ,25-dihydroxy-19-norvitamin D3 analogs with modifications in both the A-ring and the side chain)

IT 2568-33-4P 17689-66-6P 192573-37-8P 681433-60-3P
681433-62-5P 681433-78-3P 681433-79-4P 681433-80-7P
681433-81-8P 681433-91-0P 681433-92-1P 681433-93-2P
681433-94-3P 681433-95-4P 681433-98-7P 681433-99-8P
681434-00-4P 681434-01-5P 681434-02-6P 681434-03-7P
681434-04-8P 681434-05-9P 681434-06-0P
681434-08-2P 681434-09-3P 681434-10-6P 681434-11-7P
681434-12-8P 681434-13-9P 681434-14-0P
681434-16-2P 681434-17-3P 681434-18-4P 681434-19-5P
681434-22-0P 681830-90-0P 681830-91-1P 681830-92-2P
681831-07-2P 681831-08-3P 681831-10-7P
681856-70-2P 681856-71-3P 884488-07-7P
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897923-06-7P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP
(Preparation); RACT (Reactant or reagent)
(synthesis and vitamin D receptor binding activity of new
1 α ,25-dihydroxy-19-norvitaminD3 analogs with
modifications in both the A-ring and the side chain)

REFERENCE COUNT: 33 THERE ARE 33 CITED REFERENCES AVAILABLE
FOR THIS RECORD. ALL CITATIONS AVAILABLE
IN THE RE FORMAT

L19 ANSWER 3 OF 6 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2004:522172 HCAPLUS

DOCUMENT NUMBER: 141:185222

TITLE: Two-dimensional alanine scanning mutational
analysis of the interaction between the
vitamin D receptor and its ligands: studies of
A-ring modified 19-norvitamin D analogs
AUTHOR(S): Shimizu, Masato; Yamamoto, Keiko; Mihori,
Mika; Iwasaki, Yukiko; Morizono, Daisuke;
Yamada, Sachiko

CORPORATE SOURCE: Institute of Biomaterial and Bioengineering,
Tokyo Medical and Dental University, Tokyo,
101-0062, Japan

SOURCE: Journal of Steroid Biochemistry and Molecular
Biology (2004), 89-90(1-5), 75-81
CODEN: JSBBEZ; ISSN: 0960-0760

PUBLISHER: Elsevier Science Ltd.

DOCUMENT TYPE: Journal

LANGUAGE: English

AB To clarify the structure-function relationship (SFR) of vitamin D
analogues in terms of their interaction with the vitamin D receptor
(VDR), we have proposed a new approach, two-dimensional alanine
scanning mutational anal. (2D-ASMA). In this paper, attention was
focused on the interactions around the A-ring of vitamin D. For
this purpose, we synthesized four new 2-substituted 19-norvitamin
D derivs. (3-6). The VDR affinity (3-6: 1, 5, 2 and 1/140, resp.)
and transcriptional activity (3-6: 10, 30, 2 and 0.3, resp.) of
the four compds. were evaluated relative to 1,25-(OH)2D3 (5)
(normalized to 1). Then, the transcriptional activities of
wild-type and 18 mutant VDRs induced by the four compds. (3-6)
were investigated. The results of this 18+4 2D-ASMA were
presented as a patch table, and the effects of the mutations were
analyzed in comparison with the natural hormone (1) and
2-methylene-19-nor-20-epi-1,25-(OH)2D3 (2MD, 2). Of the four
A-ring analogs, the 2 α -hydroxyethoxy derivative (3) showed
striking differences in the pattern on the patch table. From the
results, we suggest a docking mode of this compound (3) in which the
A-ring adopts the α conformation.

IT 737757-31-2P

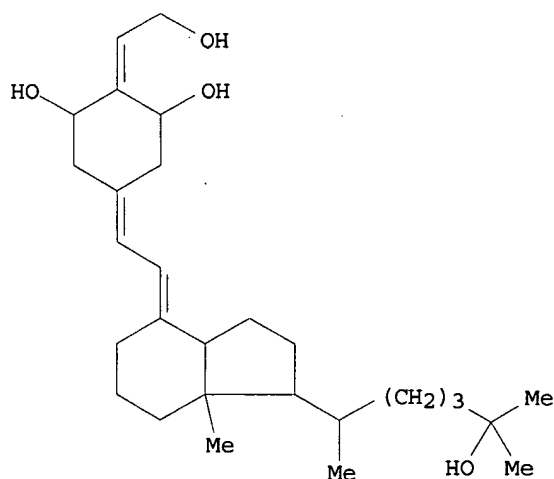
RL: BSU (Biological study, unclassified); PRP (Properties); SPN
(Synthetic preparation); BIOL (Biological study); PREP

(Preparation)

(two-dimensional alanine scanning mutational anal. of
interaction between the vitamin D receptor and its ligands:
studies of A-ring modified 19-norvitamin D analogs)

RN 737757-31-2 HCAPLUS

CN 19-Nor-9,10-secocholesta-5,7-diene-1,3,25-triol,
2-(2-hydroxyethylidene)-, (1 α ,2Z,3 β ,7E)- (9CI) (CA
INDEX NAME)



IT 736982-52-8P 736982-53-9P 736982-54-0P

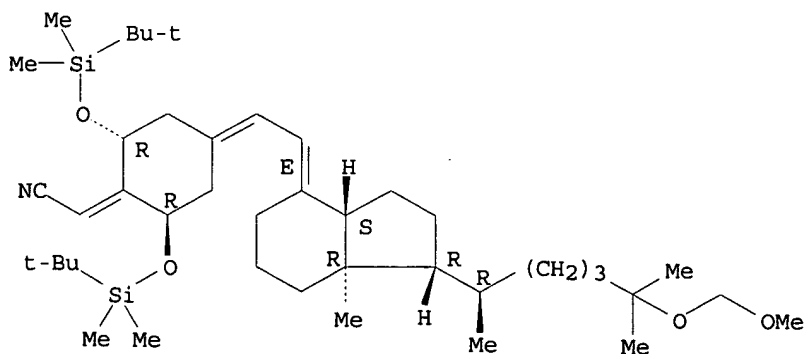
RL: RCT (Reactant); SPN (Synthetic preparation); PREP
(Preparation); RACT (Reactant or reagent)

(two-dimensional alanine scanning mutational anal. of
interaction between the vitamin D receptor and its ligands:
studies of A-ring modified 19-norvitamin D analogs)

RN 736982-52-8 HCAPLUS

CN Acetonitrile, [(1 α ,3 β ,7E)-1,3-bis[[[(1,1-
dimethylethyl)dimethylsilyl]oxy]-25-(methoxymethoxy)-19-nor-9,10-
secocholesta-5,7-dien-2-ylidene]- (9CI) (CA INDEX NAME)

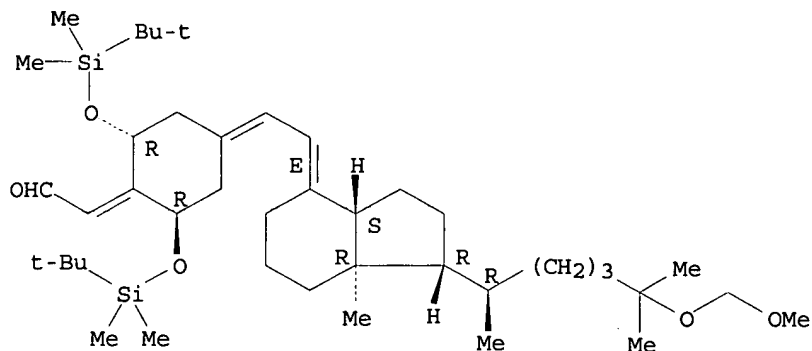
Absolute stereochemistry.
Double bond geometry as shown.



RN 736982-53-9 HCAPLUS

CN Acetaldehyde, [(1 α ,3 β ,7E)-1,3-bis[[[(1,1-
dimethylethyl)dimethylsilyl]oxy]-25-(methoxymethoxy)-19-nor-9,10-
secocholesta-5,7-dien-2-ylidene]- (9CI) (CA INDEX NAME)

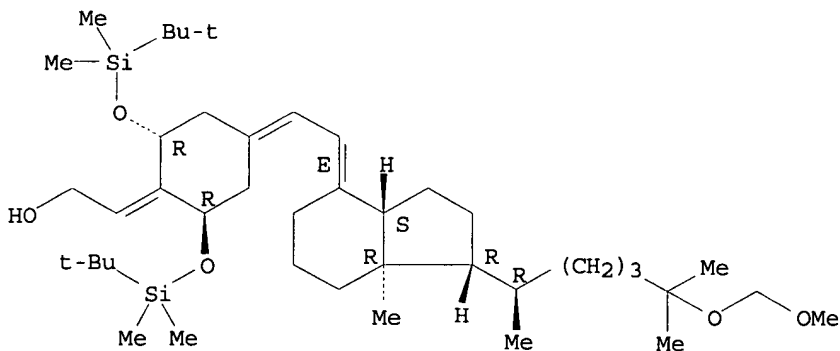
Absolute stereochemistry.
Double bond geometry as shown.



RN 736982-54-0 HCAPLUS

CN Ethanol, [(1 α ,3 β ,7E)-1,3-bis[[(1,1-dimethylethyl)dimethylsilyl]oxy]-25-(methoxymethoxy)-19-nor-9,10-secocholesta-5,7-dien-2-ylidene]-(9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



CC 2-2 (Mammalian Hormones)

IT 681830-58-0P 681830-59-1P 737757-31-2P

RL: BSU (Biological study, unclassified); PRP (Properties); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)

(two-dimensional alanine scanning mutational anal. of interaction between the vitamin D receptor and its ligands: studies of A-ring modified 19-norvitamin D analogs)

IT 736982-50-6P 736982-51-7P 736982-52-8P

736982-53-9P 736982-54-0P 737757-32-3P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(two-dimensional alanine scanning mutational anal. of interaction between the vitamin D receptor and its ligands: studies of A-ring modified 19-norvitamin D analogs)

REFERENCE COUNT: 23 THERE ARE 23 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L19 ANSWER 4 OF 6 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2004:333691 HCAPLUS

DOCUMENT NUMBER: 140:357542

TITLE: Preparation of 2,2-di-substituted

INVENTOR(S): 1 α ,25-dihydroxy-19-norvitamin D
 derivatives as pharmaceuticals
 Yamada, Sachiko; Shimizu, Masato; Iwasaki,
 Yukiko
 PATENT ASSIGNEE(S): Chugai Seiyaku Kabushiki Kaisha, Japan
 SOURCE: PCT Int. Appl., 168 pp.
 CODEN: PIXXD2
 DOCUMENT TYPE: Patent
 LANGUAGE: Japanese
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004033420	A1	20040422	WO 2003-JP13053	2003 1010

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA,
 CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES,
 FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE,
 KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG,
 MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO,
 RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ,
 UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
 RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM,
 AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ,
 DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL,
 PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN,
 GQ, GW, ML, MR, NE, SN, TD, TG

AU 2003271171	A1	20040504	AU 2003-271171	2003 1010
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EP 1559708	A1	20050803	EP 2003-751451	2003 1010
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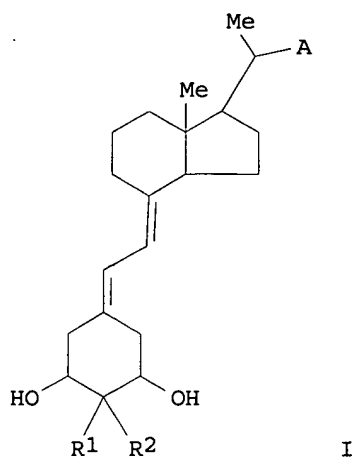
US 2006160779	A1	20060720	US 2005-530903	2005 0930
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PRIORITY APPLN. INFO.:	JP 2002-297366	A	2002 1010
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JP 2003-24183	A	2003 1031
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WO 2003-JP13053	W	2003 1010
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OTHER SOURCE(S): MARPAT 140:357542
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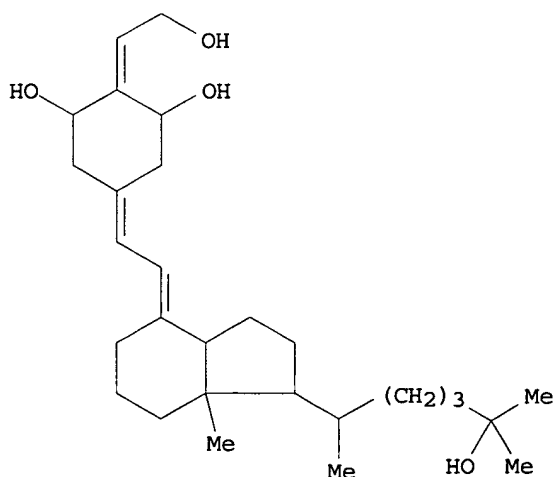
AB The title compds. I [R1 and R2 are the same or different and each represents hydroxy, etc.; and A represents hydrogen, unsubstituted linear or branched alkyl, etc.] are prepared. The bioactivity of the title compds. was demonstrated. A process for preparing I is disclosed.

IT 681830-60-4P 681830-61-5P 681830-66-0P
681830-67-1P 681830-74-0P 681830-75-1P
681830-84-2P 681830-85-3P

RL: PAC (Pharmacological activity); SPN (Synthetic preparation);
THU (Therapeutic use); BIOL (Biological study); PREP
(Preparation); USES (Uses)
(preparation of 2,2-di-substituted 1 α ,25-dihydroxy-19-
norvitamin D derivs. as pharmaceuticals)

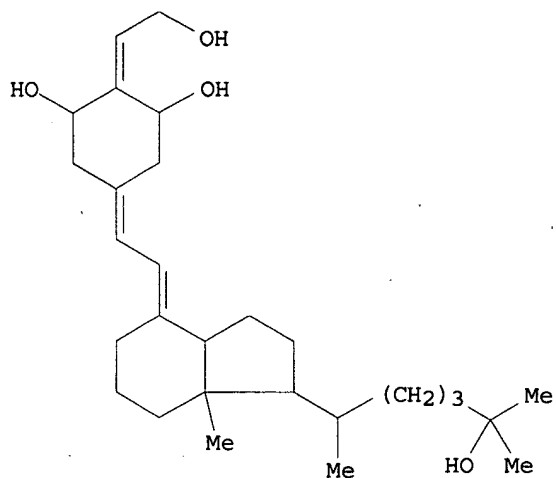
RN 681830-60-4 HCAPLUS

CN 19-Nor-9,10-secocholesta-5,7-diene-1,3,25-triol,
2-(2-hydroxyethylidene)-, (1 α ,2E,3 β ,7E,20S)- (9CI) (CA
INDEX NAME)

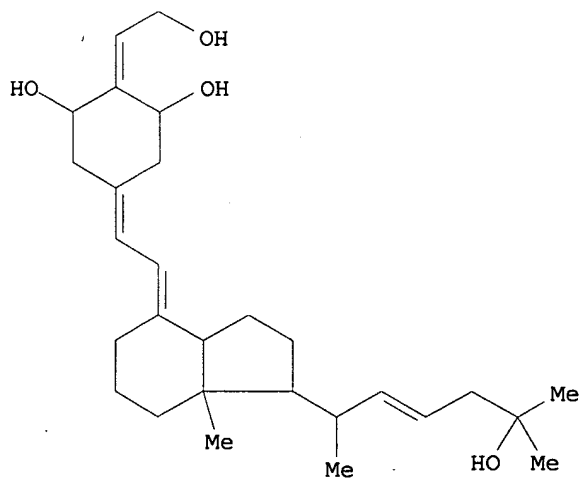


RN 681830-61-5 HCAPLUS

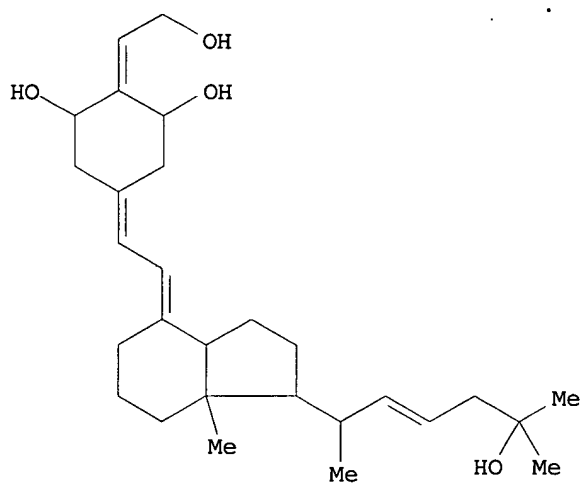
CN 19-Nor-9,10-secocholesta-5,7-diene-1,3,25-triol,
2-(2-hydroxyethylidene)-, (1 α ,2Z,3 β ,7E,20S)- (9CI) (CA
INDEX NAME)



RN 681830-66-0 HCAPLUS
 CN 19-Nor-9,10-secocholesta-5,7,22-triene-1,3,25-triol,
 2-(2-hydroxyethylidene)-, (1 α ,2E,3 β ,7E,22E)- (9CI) (CA
 INDEX NAME)

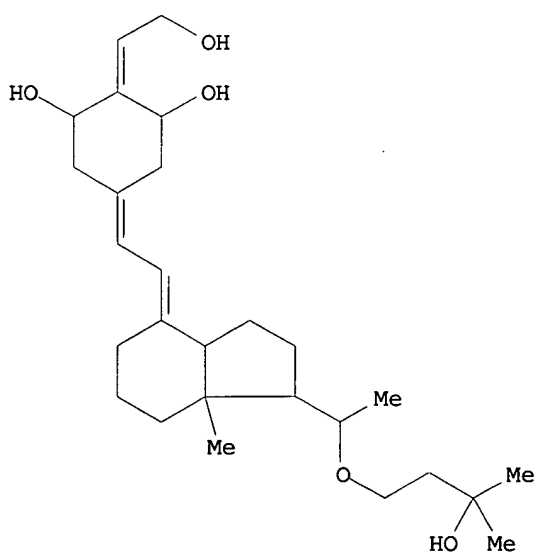


RN 681830-67-1 HCAPLUS
 CN 19-Nor-9,10-secocholesta-5,7,22-triene-1,3,25-triol,
 2-(2-hydroxyethylidene)-, (1 α ,2Z,3 β ,7E,22E)- (9CI) (CA
 INDEX NAME)



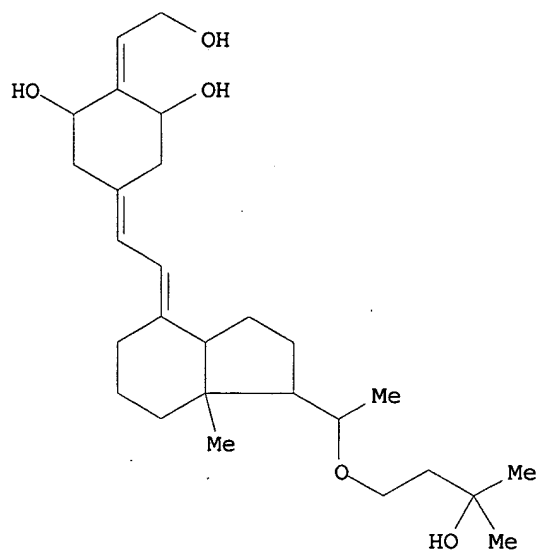
RN 681830-74-0 HCAPLUS

CN 1,3-Cyclohexanediol, 2-(2-hydroxyethylidene)-5-[[octahydro-1-[1-(3-hydroxy-3-methylbutoxy)ethyl]-7a-methyl-4H-inden-4-ylidene]ethylidene]-, stereoisomer (9CI) (CA INDEX NAME)



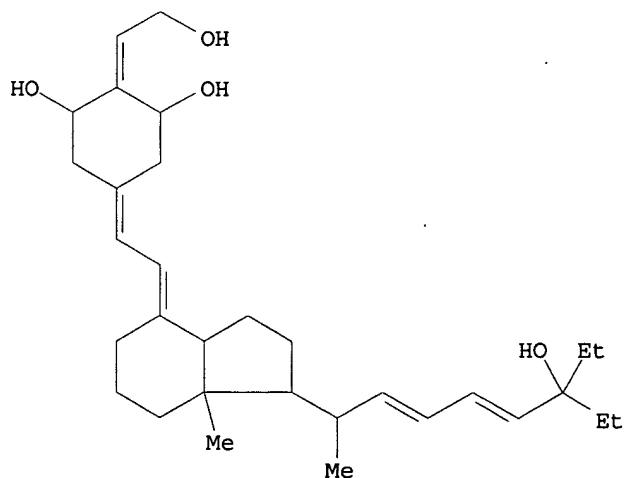
RN 681830-75-1 HCAPLUS

CN 1,3-Cyclohexanediol, 2-(2-hydroxyethylidene)-5-[[octahydro-1-[1-(3-hydroxy-3-methylbutoxy)ethyl]-7a-methyl-4H-inden-4-ylidene]ethylidene]-, stereoisomer (9CI) (CA INDEX NAME)



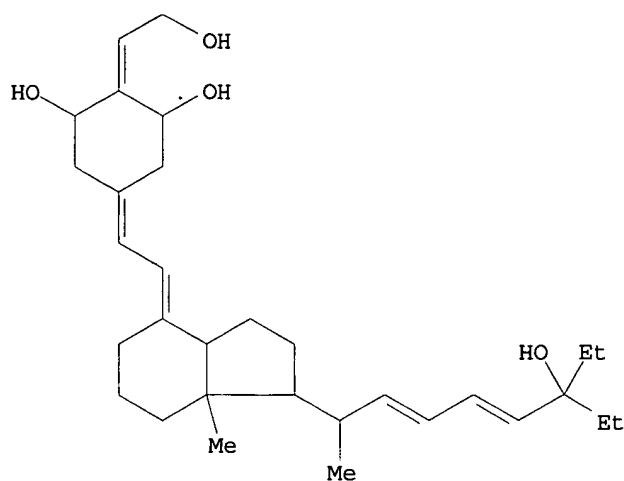
RN 681830-84-2 HCAPLUS

CN 1,3-Cyclohexanediol, 5-[[1-(6-ethyl-6-hydroxy-1-methyl-2,4-octadienyl)octahydro-7a-methyl-4H-inden-4-ylidene]ethylidene]-2-(2-hydroxyethylidene)-, stereoisomer (9CI) (CA INDEX NAME)



RN 681830-85-3 HCAPLUS

CN 1,3-Cyclohexanediol, 5-[[1-(6-ethyl-6-hydroxy-1-methyl-2,4-octadienyl)octahydro-7a-methyl-4H-inden-4-ylidene]ethylidene]-2-(2-hydroxyethylidene)-, stereoisomer (9CI) (CA INDEX NAME)



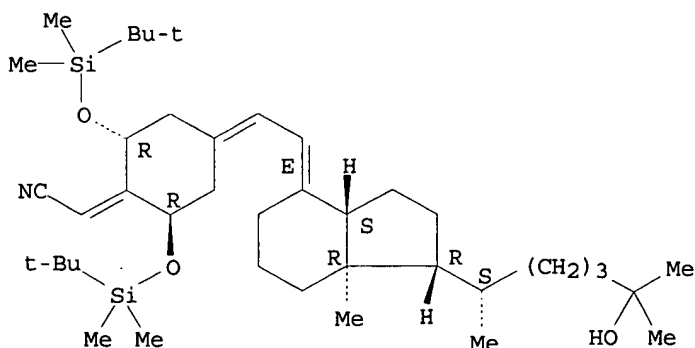
IT 681433-77-2P 681434-05-9P 681434-06-0P
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 681831-07-2P 681831-08-3P 681831-10-7P
 681856-69-9P 681856-70-2P 681856-71-3P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP
 (Preparation); RACT (Reactant or reagent)
 (preparation of 2,2-di-substituted 1a,25-dihydroxy-19-
 norvitamin D derivs. as pharmaceuticals)

RN 681433-77-2 HCAPLUS

CN Acetonitrile, [(2R,6R)-2,6-bis[[[(1,1-dimethylethyl)dimethylsilyl]oxy]-4-[(2E)-[(1R,3aS,7aR)-octahydro-1-[(1S)-5-hydroxy-1,5-dimethylhexyl]-7a-methyl-4H-inden-4-ylidene]ethylidene]cyclohexylidene]- (9CI) (CA INDEX NAME)

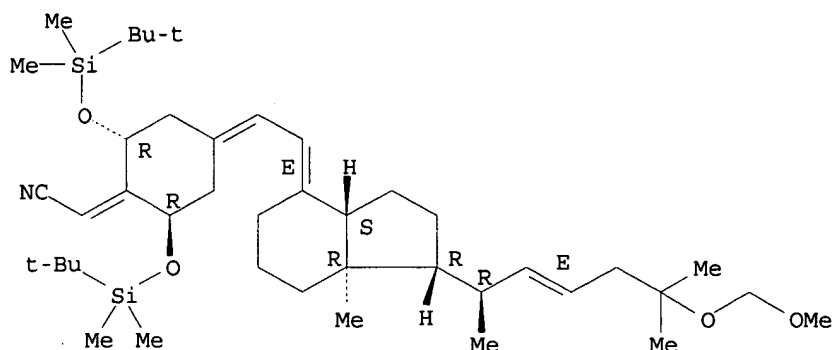
Absolute stereochemistry.
 Double bond geometry as shown.



RN 681434-05-9 HCAPLUS

CN Acetonitrile, [(2R,6R)-2,6-bis[[[(1,1-dimethylethyl)dimethylsilyl]oxy]-4-[(2E)-[(1R,3aS,7aR)-octahydro-1-[(1R,2E)-5-(methoxymethoxy)-1,5-dimethyl-2-hexenyl]-7a-methyl-4H-inden-4-ylidene]ethylidene]cyclohexylidene]- (9CI) (CA INDEX NAME)

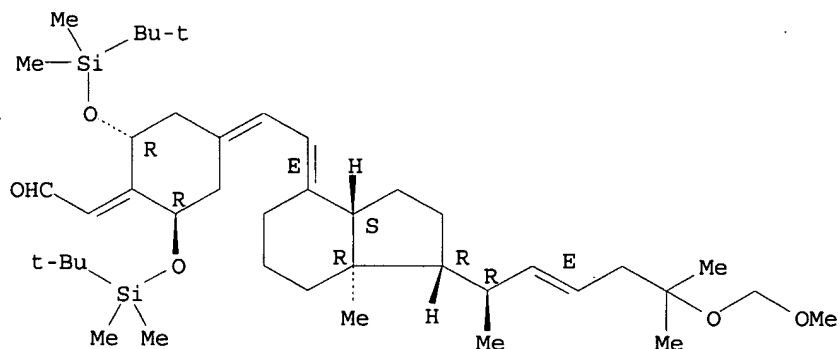
Absolute stereochemistry.
 Double bond geometry as shown.



RN 681434-06-0 HCAPLUS

CN Acetaldehyde, [(2R,6R)-2,6-bis[[[1,1-dimethylethyl]dimethylsilyl]oxy]-4-[(2E)-[(1R,3aS,7aR)-octahydro-1-[(1R,2E)-5-(methoxymethoxy)-1,5-dimethyl-2-hexenyl]-7a-methyl-4H-inden-4-ylidene]ethylidene]cyclohexylidene]- (9CI) (CA INDEX NAME)

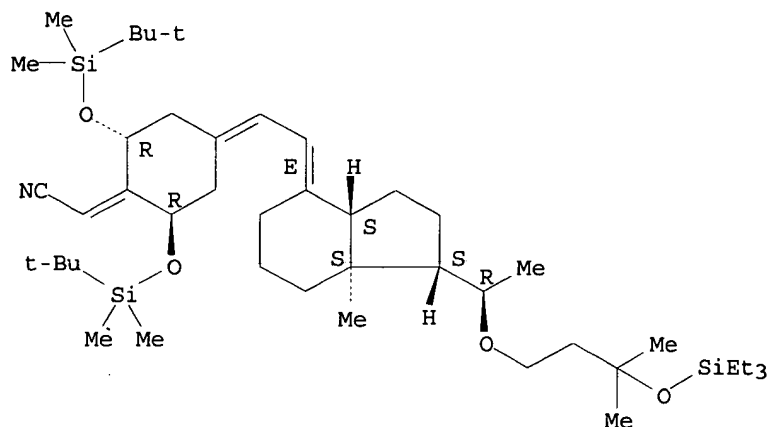
Absolute stereochemistry.
Double bond geometry as shown.



RN 681434-13-9 HCAPLUS

CN Acetonitrile, [(2R,6R)-2,6-bis[[[1,1-dimethylethyl]dimethylsilyl]oxy]-4-[(2E)-[(1S,3aS,7aS)-octahydro-7a-methyl-1-[(1R)-1-[3-methyl-3-[(triethylsilyl)oxy]butoxy]ethyl]-4H-inden-4-ylidene]ethylidene]cyclohexylidene]- (9CI) (CA INDEX NAME)

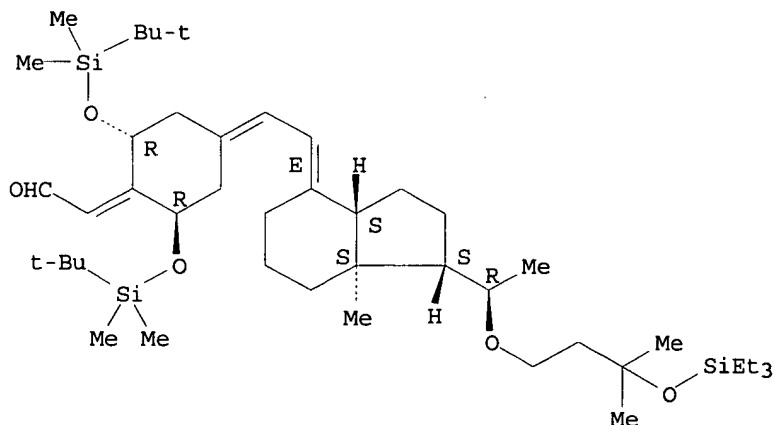
Absolute stereochemistry.
Double bond geometry as shown.



RN 681434-14-0 HCAPLUS

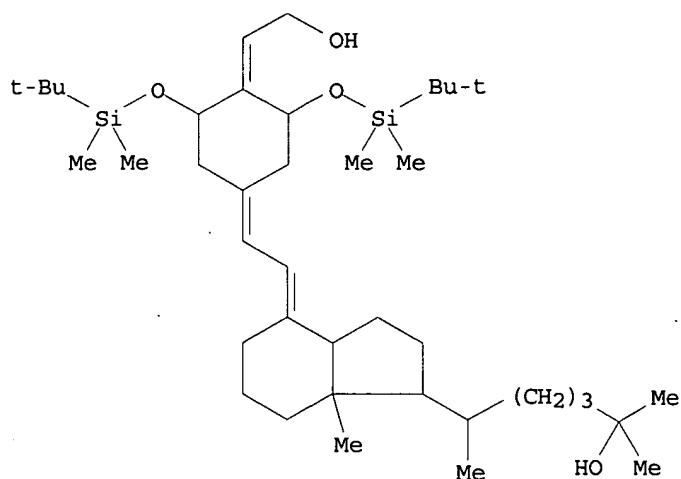
CN Acetaldehyde, [(2R,6R)-2,6-bis[[[(1,1-dimethylethyl)dimethylsilyl]oxy]-4-[(2E)-[(1S,3aS,7aS)-octahydro-7a-methyl-1-[(1R)-1-[3-methyl-3-[(triethylsilyl)oxy]butoxy]ethyl]-4H-inden-4-ylidene]ethylidene]cyclohexylidene]-(9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



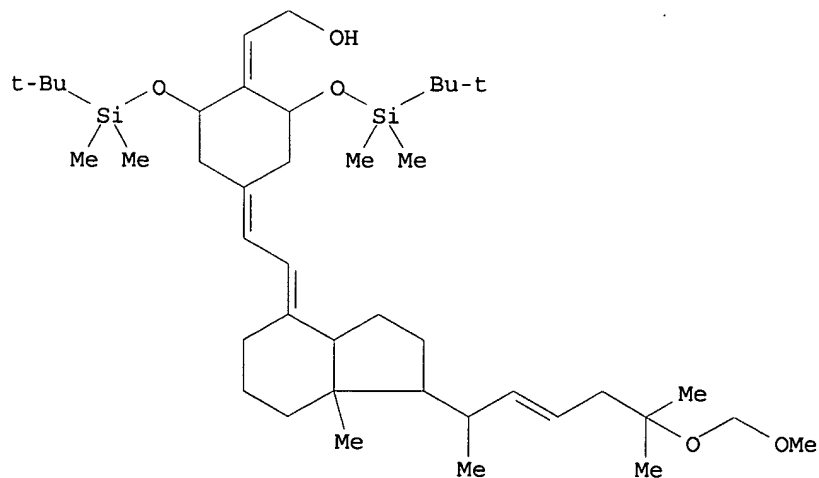
RN 681831-02-7 HCAPLUS

CN 19-Nor-9,10-secocholesta-5,7-dien-25-ol,1,3-bis[[[(1,1-dimethylethyl)dimethylsilyl]oxy]-2-(2-hydroxyethylidene)-, (1α,2E,3β,7E,20S) - (9CI) (CA INDEX NAME)



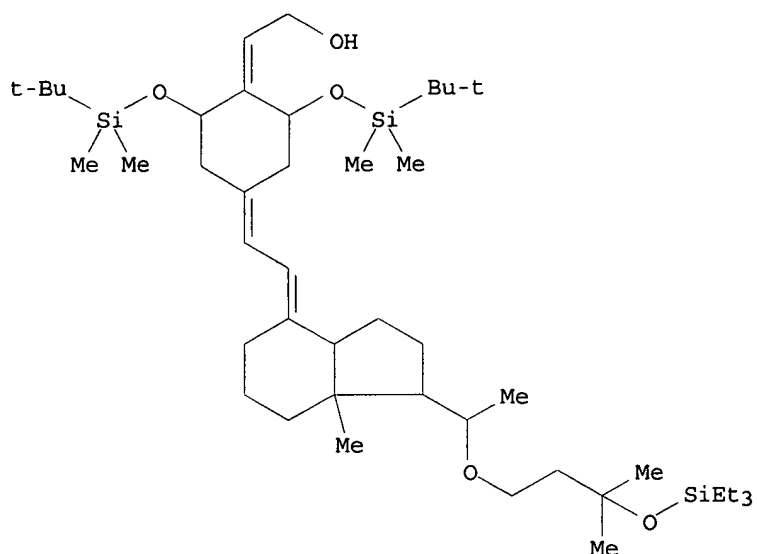
RN 681831-07-2 HCAPLUS

CN Ethanol, 2-[(1 α ,3 β ,7E,22E)-1,3-bis[[1,1-dimethylethyl]dimethylsilyl]oxy]-25-(methoxymethoxy)-19-nor-9,10-secocholesta-5,7,22-trien-2-ylidene]-, (2E)- (9CI) (CA INDEX NAME)



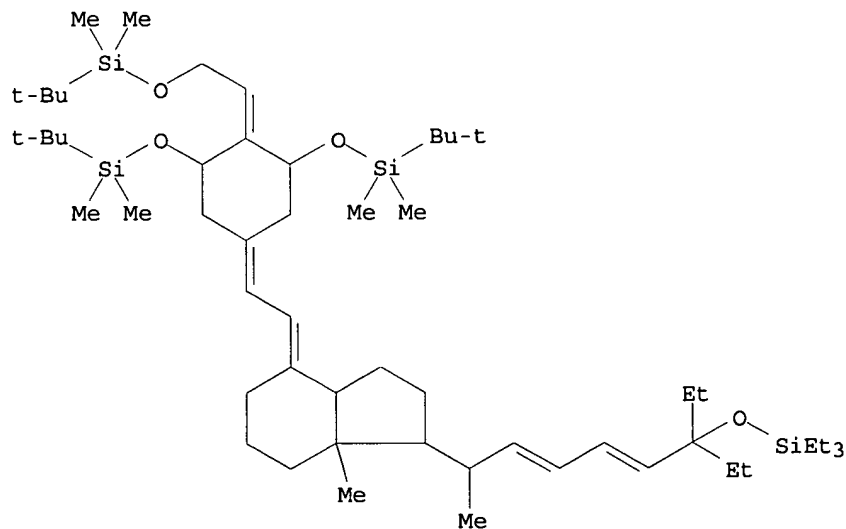
RN 681831-08-3 HCAPLUS

CN Ethanol, 2-[2,6-bis[[1,1-dimethylethyl]dimethylsilyl]oxy]-4-[[octahydro-7a-methyl-1-[1-[3-methyl-3-[(triethylsilyl)oxy]butoxy]ethyl]-4H-inden-4-ylidene]ethylidene]cyclohexylidene]-, stereoisomer (9CI) (CA INDEX NAME)



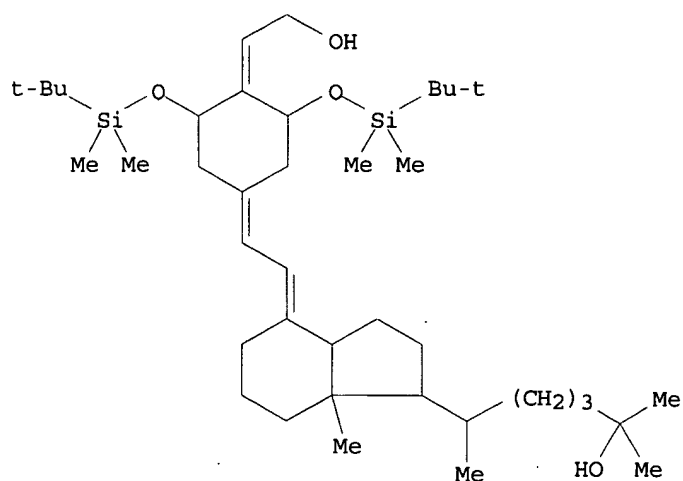
RN 681831-10-7 HCAPLUS

CN Silane, [[(1R,3R)-2-[(1E)-2-[[[(1,1-dimethylethyl)dimethylsilyl]oxy]ethylidene]-5-[(2E)-[(1R,3aS,7aR)-1-[(1R,2E,4E)-6-ethyl-1-methyl-6-[(triethylsilyl)oxy]-2,4-octadienyl]octahydro-7a-methyl-4H-inden-4-ylidene]ethylidene]-1,3-cyclohexanediyl]bis(oxy)]bis[(1,1-dimethylethyl)dimethyl- (9CI) (CA INDEX NAME)



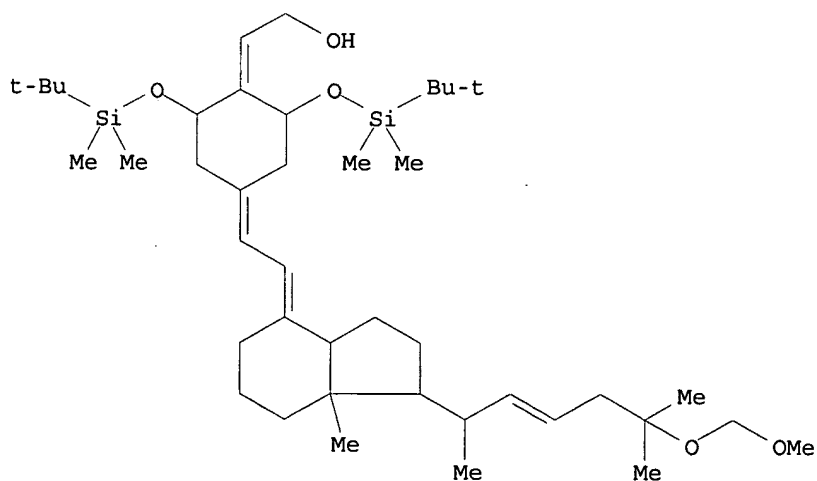
RN 681856-69-9 HCAPLUS

CN 19-Nor-9,10-secocholesta-5,7-dien-25-ol,1,3-bis[[[(1,1-dimethylethyl)dimethylsilyl]oxy]-2-(hydroxyethylidene)-, (1α,2Z,3β,7E,20S)- (9CI) (CA INDEX NAME)



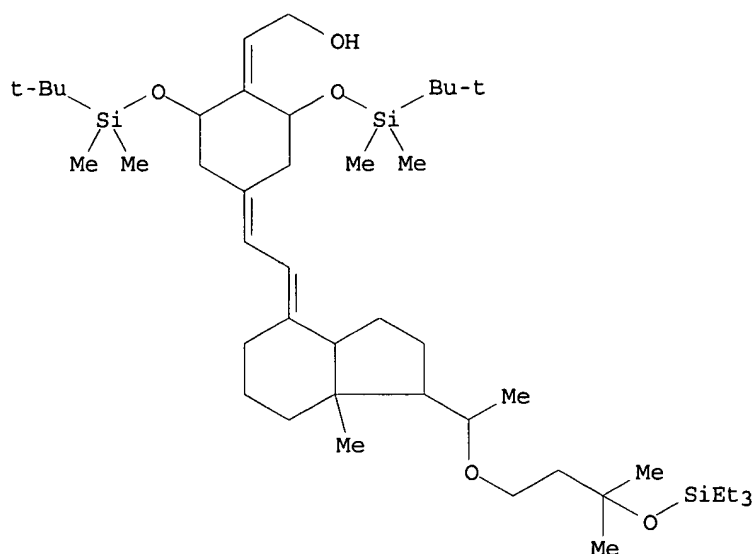
RN 681856-70-2 HCAPLUS

CN Ethanol, 2-[(1 α ,3 β ,7E,22E)-1,3-bis[[(1,1-dimethylethyl)dimethylsilyl]oxy]-25-(methoxymethoxy)-19-nor-9,10-secocholesta-5,7,22-trien-2-ylidene]-, (2Z)-(9CI) (CA INDEX NAME)



RN 681856-71-3 HCAPLUS

CN Ethanol, 2-[2,6-bis[[(1,1-dimethylethyl)dimethylsilyl]oxy]-4-[[octahydro-7a-methyl-1-[1-[3-methyl-3-[(triethylsilyl)oxy]butoxy]ethyl]-4H-inden-4-ylidene]ethylidene]cyclohexylidene]-, stereoisomer (9CI) (CA INDEX NAME)



IC ICM C07C401-00

ICS A61K031-59; A61P035-00; A61P037-02; A61P043-00

CC 32-7 (Steroids)

Section cross-reference(s): 1, 63

IT 681433-59-0P 681433-60-3P 681830-46-6P 681830-47-7P
 681830-48-8P 681830-49-9P 681830-50-2P 681830-51-3P
 681830-52-4P 681830-53-5P 681830-55-7P 681830-56-8P
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681830-61-5P 681830-62-6P 681830-63-7P 681830-64-8P
 681830-65-9P **681830-66-0P** **681830-67-1P**
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RL: PAC (Pharmacological activity); SPN (Synthetic preparation);
 THU (Therapeutic use); BIOL (Biological study); PREP
 (Preparation); USES (Uses)

(preparation of 2,2-di-substituted 1 α ,25-dihydroxy-19-norvitamin D derivs. as pharmaceuticals)

IT 139131-74-1P 139131-75-2P 139131-76-3P 147725-63-1P
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681856-70-2P 681856-71-3P 681857-02-3P
681857-03-4P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP
(Preparation); RACT (Reactant or reagent)
(preparation of 2,2-di-substituted 1 α ,25-dihydroxy-19-
norvitamin D derivs. as pharmaceuticals)

REFERENCE COUNT: 17 THERE ARE 17 CITED REFERENCES AVAILABLE
FOR THIS RECORD. ALL CITATIONS AVAILABLE
IN THE RE FORMAT

L19 ANSWER 5 OF 6 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2002:485206 HCAPLUS

DOCUMENT NUMBER: 137:217136

TITLE: 2-Ethyl and 2-Ethylidene Analogues of
1 α ,25-Dihydroxy-19-norvitamin D3:
Synthesis, Conformational Analysis, Biological
Activities, and Docking to the Modeled rVDR
Ligand Binding Domain

AUTHOR(S): Sicinski, Rafal R.; Rotkiewicz, Piotr;
Kolinski, Andrzej; Sicinska, Wanda; Prahl,
Jean M.; Smith, Connie M.; DeLuca, Hector F.

CORPORATE SOURCE: Department of Biochemistry, University of
Wisconsin, Madison, WI, 53706, USA

SOURCE: Journal of Medicinal Chemistry (2002), 45(16),
3366-3380

CODEN: JMCMAR; ISSN: 0022-2623

PUBLISHER: American Chemical Society

DOCUMENT TYPE: Journal

LANGUAGE: English

OTHER SOURCE(S): CASREACT 137:217136

AB Novel 19-nor analogs of 1 α ,25-dihydroxyvitamin D3 were
prepared and substituted at C-2 with an ethylidene group. The
synthetic pathway was via Wittig-Horner coupling of the
corresponding A-ring phosphine oxides with the protected
25-hydroxy Grundmann's ketones. Selective catalytic hydrogenation
of 2-ethylidene analogs provided the 2 α - and 2 β -Et
compds. The 2-ethylidene-19-nor compds. with a Me group from the
ethylidene moiety in a trans relationship to the C(6)-C(7) bond
(E-isomers) were more potent than the corresponding Z-isomers and
the natural hormone in binding to the vitamin D receptor. Both
geometrical isomers (E and Z) of (20S)-2-ethylidene-19-norvitamin
D3 and both 2 α -ethyl-19-norvitamins (in the 20R- and
20S-series) have much higher HL-60 differentiation activity than
does 1 α ,25-(OH)2D3. Both E-isomers (20R and 20S) of
2-ethylidene vitamins are characterized by very high calcemic
activity in rats. The three-dimensional structure model of the
rat vitamin D receptor and the computational docking of four
synthesized (20R)-19-norvitamin D3 analogs into its binding pocket
are also reported.

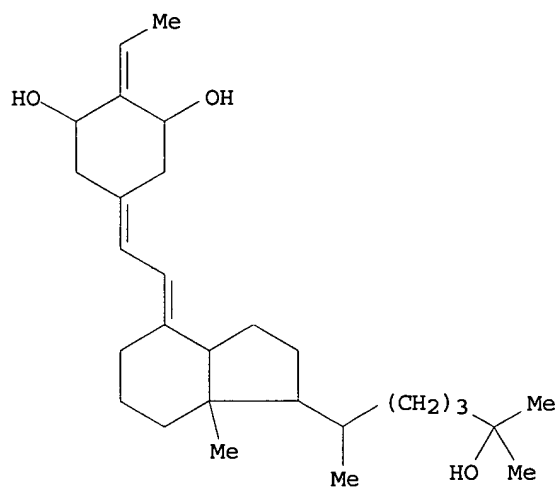
IT 377086-22-1P 377086-23-2P 377086-32-3P
377087-90-6P

RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic
preparation); BIOL (Biological study); PREP (Preparation); RACT
(Reactant or reagent)

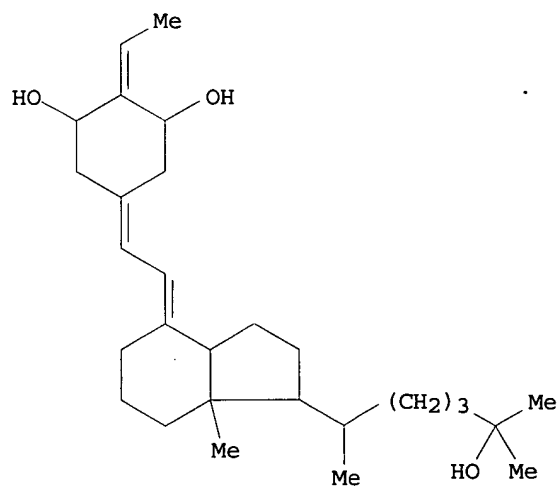
(preparation of Et and ethylidene dihydroxy-19-norvitamin D3 analogs
via Wittig-Horner, their conformation, vitamin D receptor
activity, calcium transport and mobilization activities, and
HL-60 differentiation)

RN 377086-22-1 HCAPLUS

CN 19-Nor-9,10-secocholesta-5,7-diene-1,3,25-triol,2-ethylidene-,
(1 α ,2E,3 β)- (9CI) (CA INDEX NAME)

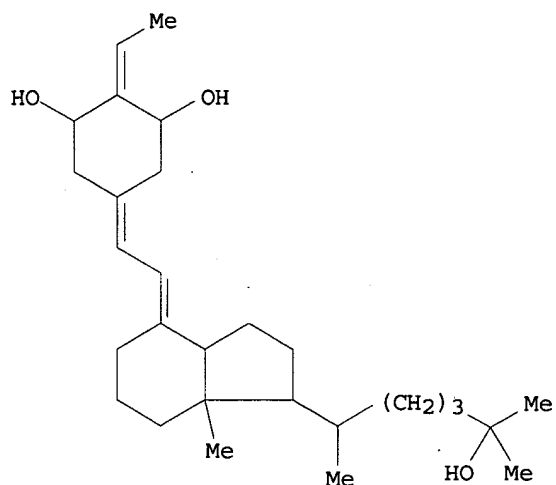


RN 377086-23-2 HCAPLUS

CN 19-Nor-9,10-secocholesta-5,7-diene-1,3,25-triol,2-ethylidene-,
(1 α ,2Z,3 β)- (9CI) (CA INDEX NAME)

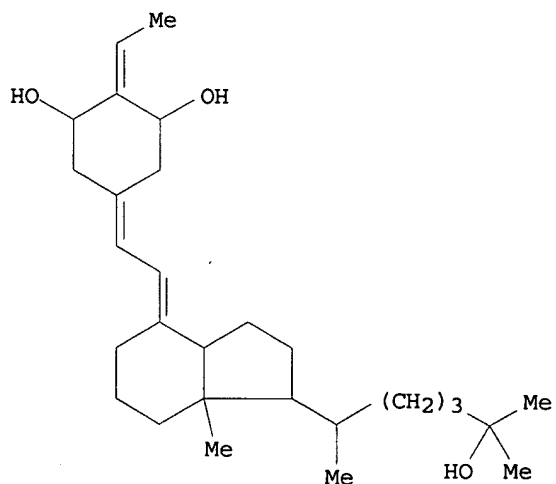
RN 377086-32-3 HCAPLUS

CN 19-Nor-9,10-secocholesta-5,7-diene-1,3,25-triol,2-ethylidene-,
(1 α ,2Z,3 β ,20S)- (9CI) (CA INDEX NAME)



RN 377087-90-6 HCAPLUS

CN 19-Nor-9,10-secocholesta-5,7-diene-1,3,25-triol,2-ethylidene-,
(1α,2E,3β,20S)- (9CI) (CA INDEX NAME)



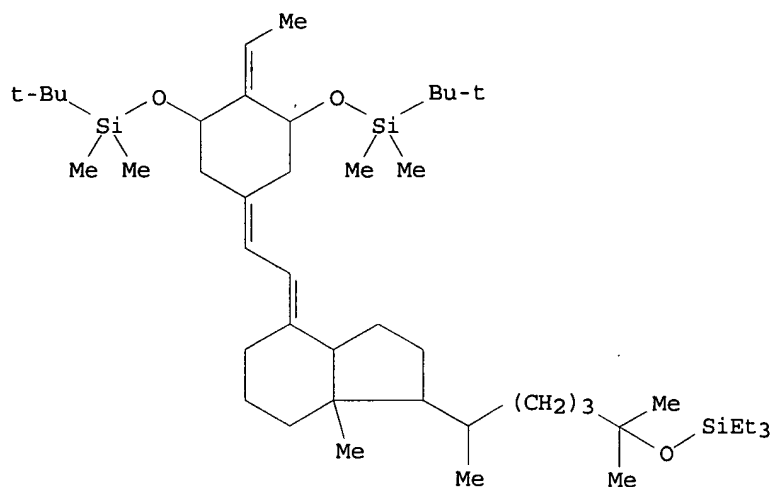
IT 377086-30-1P 455253-25-5P 455253-26-6P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP
(Preparation); RACT (Reactant or reagent)

(preparation of Et and ethylidene dihydroxy-19-norvitamin D3 analogs
via Wittig-Horner, their conformation, vitamin D receptor
activity, calcium transport and mobilization activities, and
HL-60 differentiation)

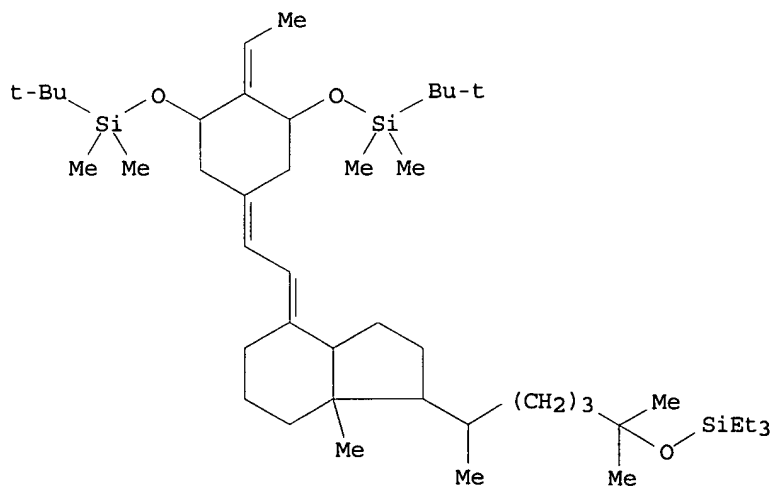
RN 377086-30-1 HCAPLUS

CN Silane, [[(1α,2E,3β,7E)-2-ethylidene-25-
[(triethylsilyl)oxy]-19-nor-9,10-secocholesta-5,7-diene-1,3-
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NAME)



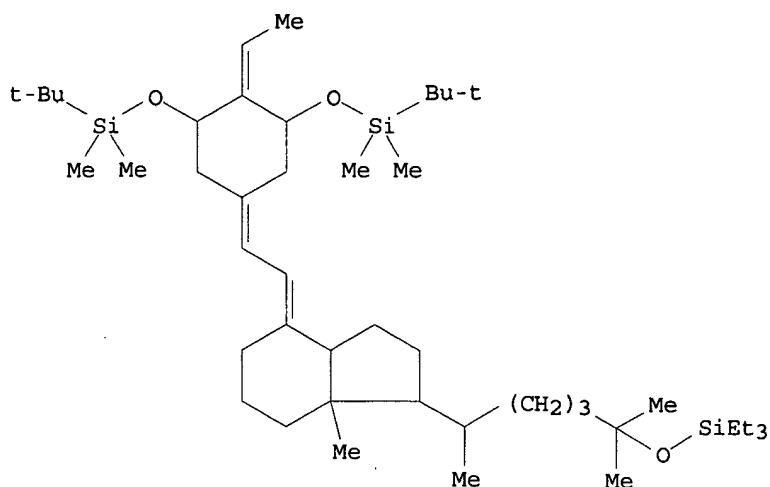
RN 455253-25-5 HCAPLUS

CN Silane, [[(1 α ,2E,3 β ,7E,20S)-2-ethylidene-25-
[(triethylsilyl)oxy]-19-nor-9,10-secocholesta-5,7-diene-1,3-
diyl]bis(oxy)]bis[(1,1-dimethylethyl)dimethyl-(9CI) (CA INDEX
NAME)



RN 455253-26-6 HCAPLUS

CN Silane, [[(1 α ,2Z,3 β ,7E,20S)-2-ethylidene-25-
[(triethylsilyl)oxy]-19-nor-9,10-secocholesta-5,7-diene-1,3-
diyl]bis(oxy)]bis[(1,1-dimethylethyl)dimethyl-(9CI) (CA INDEX
NAME)



CC 32-7 (Steroids)
 Section cross-reference(s): 1
 IT 377086-22-1P 377086-23-2P 377086-32-3P
 377087-90-6P
 RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent)
 (preparation of Et and ethylidene dihydroxy-19-norvitamin D3 analogs via Wittig-Horner, their conformation, vitamin D receptor activity, calcium transport and mobilization activities, and HL-60 differentiation)
 IT 376353-72-9P 376353-73-0P 376353-74-1P 377086-26-5P
 377086-27-6P 377086-28-7P 377086-29-8P 377086-30-1P
 455253-25-5P 455253-26-6P
 RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
 (preparation of Et and ethylidene dihydroxy-19-norvitamin D3 analogs via Wittig-Horner, their conformation, vitamin D receptor activity, calcium transport and mobilization activities, and HL-60 differentiation)
 REFERENCE COUNT: 82 THERE ARE 82 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

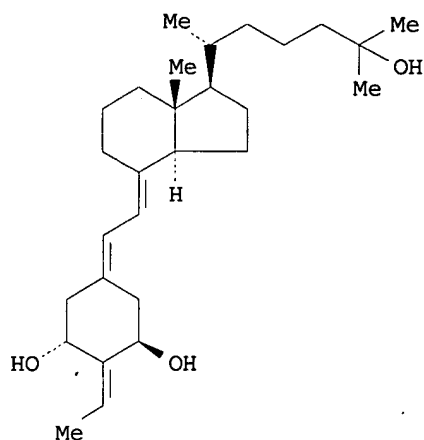
L19 ANSWER 6 OF 6 HCAPLUS COPYRIGHT 2006 ACS on STN
 ACCESSION NUMBER: 2001:886060 HCAPLUS
 DOCUMENT NUMBER: 136:6208
 TITLE: Preparation and formulation of 2-ethyl and 2-ethylidene-19-nor-vitamin D compounds
 INVENTOR(S): Deluca, Hector F.; Sicinski, Rafal R.
 PATENT ASSIGNEE(S): Wisconsin Alumni Research Foundation, USA
 SOURCE: PCT Int. Appl., 57 pp.
 CODEN: PIXXD2
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001092221	A1	20011206	WO 2001-US17662	20010531

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 MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL,
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 PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR,
 NE, SN, TD, TG

CA 2410880	AA	20011206	CA 2001-2410880	2001 0531
US 2003013691	A1	20030116	US 2001-871227	2001 0531
US 6806262	B2	20041019		
EP 1286962	A1	20030305	EP 2001-939792	2001 0531
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EP 1524264	A2	20050420	EP 2005-1268	2001 0531
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US 6992074	B2	20060131		
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PRIORITY APPLN. INFO.:			US 2000-208199P	P 2000 0531
			EP 2001-939792	A3 2001 0531
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			WO 2001-US17662	W 2001 0531
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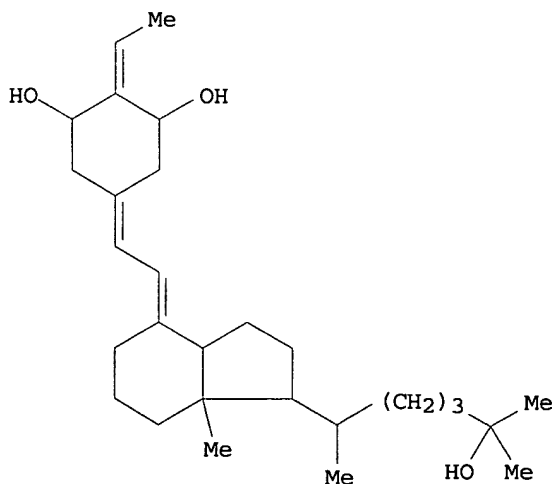
AB Biol. active 19-nor vitamin D analogs substituted at C-2 in the A-ring with an ethylidene or an Et group are prepared. These compounds have preferential activity on mobilizing calcium from bone and either high or normal intestinal calcium transport activity which allows their in vivo administration for the treatment of metabolic bone diseases where bone loss is a major concern. These compounds are also characterized by high cell differentiation activity. Thus, I was prepared and showed high calcemic activity when tested in vivo in rats.

IT 377086-22-1P 377086-23-2P 377086-32-3P
377087-90-6P

RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(preparation of biol. active 2-Et and 2-ethylidene-19-norvitamin D compounds.)

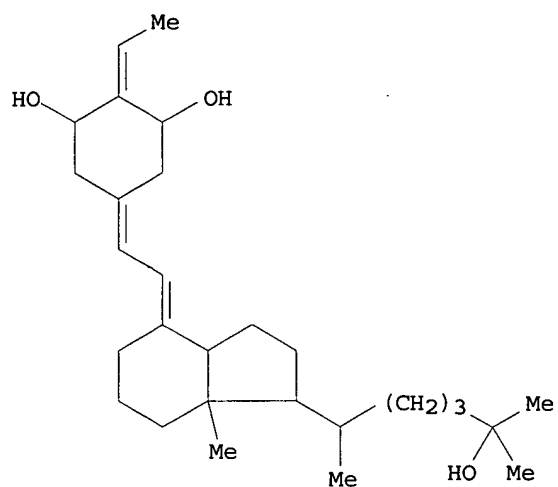
RN 377086-22-1 HCAPLUS

CN 19-Nor-9,10-secocholesta-5,7-diene-1,3,25-triol,2-ethylidene-,
(1 α ,2E,3 β)- (9CI) (CA INDEX NAME)

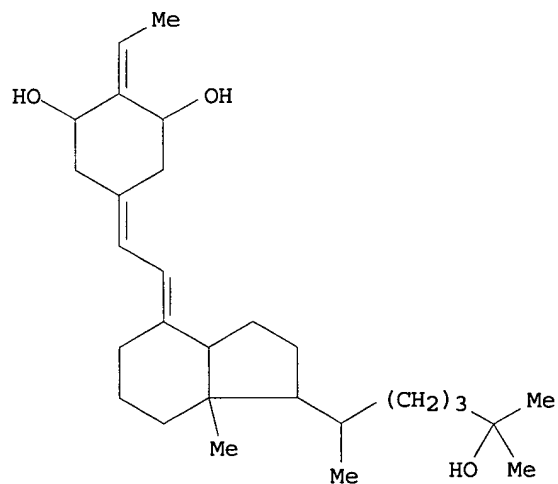


RN 377086-23-2 HCAPLUS

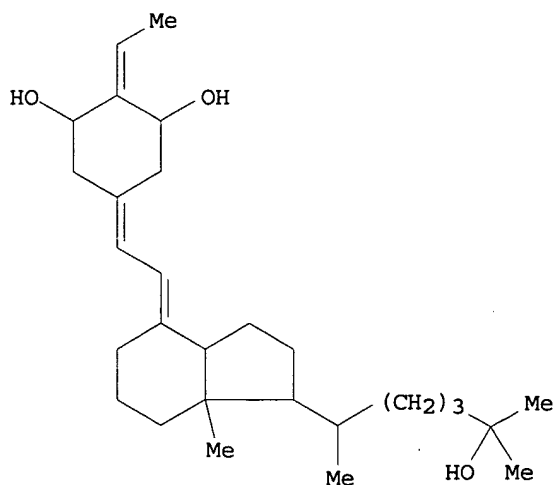
CN 19-Nor-9,10-secocholesta-5,7-diene-1,3,25-triol,2-ethylidene-,
(1 α ,2Z,3 β)- (9CI) (CA INDEX NAME)



RN 377086-32-3 HCAPLUS
CN 19-Nor-9,10-secocholesta-5,7-diene-1,3,25-triol,2-ethylidene-,
(1 α ,2Z,3 β ,20S) - (9CI) (CA INDEX NAME)



RN 377087-90-6 HCAPLUS
CN 19-Nor-9,10-secocholesta-5,7-diene-1,3,25-triol,2-ethylidene-,
(1 α ,2E,3 β ,20S) - (9CI) (CA INDEX NAME)

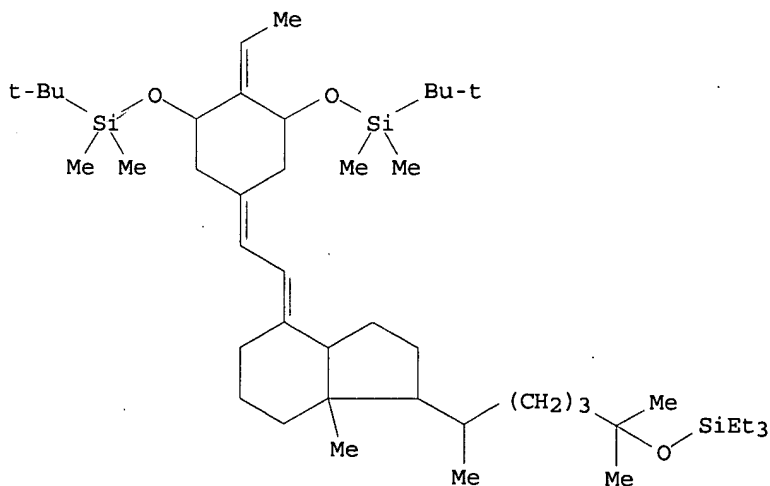


IT 377086-30-1P 377086-31-2P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent) (preparation of biol. active 2-Et and 2-ethylidene-19-norvitamin D compds.)

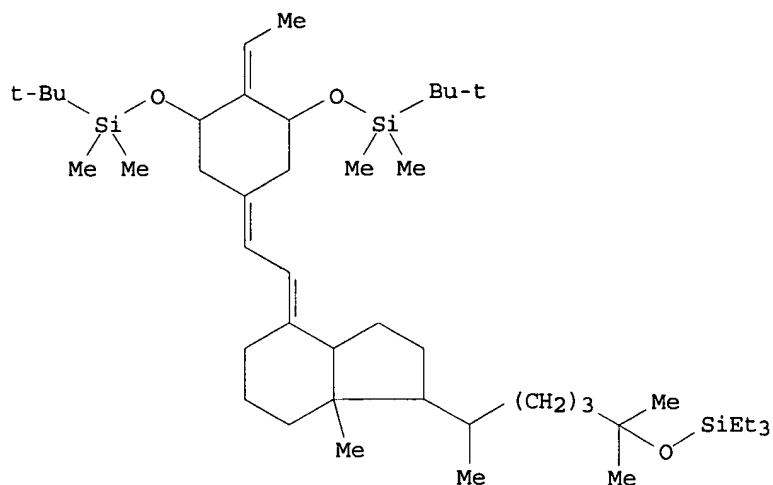
RN 377086-30-1 HCAPLUS

CN Silane, [[(1 α ,2E,3 β ,7E)-2-ethylidene-25-[(triethylsilyl)oxy]-19-nor-9,10-secocholesta-5,7-diene-1,3-diyl]bis(oxy)]bis[(1,1-dimethylethyl)dimethyl-(9CI) (CA INDEX NAME)



RN 377086-31-2 HCAPLUS

CN Silane, [[(1 α ,2Z,3 β ,7E)-2-ethylidene-25-[(triethylsilyl)oxy]-19-nor-9,10-secocholesta-5,7-diene-1,3-diyl]bis(oxy)]bis[(1,1-dimethylethyl)dimethyl-(9CI) (CA INDEX NAME)



IC ICM C07C401-00

ICS A61K031-59

CC 32-7 (Steroids)

Section cross-reference(s): 1, 63

IT 377086-22-1P 377086-23-2P 377086-32-3P

377087-90-6P

RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)

(preparation of biol. active 2-Et and 2-ethylidene-19-norvitamin D compds.)

IT 135711-62-5P 141404-07-1P 141404-08-2P 376353-72-9P

376353-73-0P 376353-74-1P 376353-75-2P 376353-76-3P

376353-77-4P 376353-78-5P 376353-79-6P 377086-26-5P

377086-27-6P 377086-28-7P 377086-29-8P 377086-30-1P

377086-31-2P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP

(Preparation); RACT (Reactant or reagent)

(preparation of biol. active 2-Et and 2-ethylidene-19-norvitamin D compds.)

REFERENCE COUNT:

2

THERE ARE 2 CITED REFERENCES AVAILABLE
FOR THIS RECORD. ALL CITATIONS AVAILABLE
IN THE RE FORMAT

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